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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<b>(54) Title:</b> ELONGIN A AND C FUNCTIONAL DOMAINS  <b>(57) Abstract</b>  The functional domains of Elongin A having transcriptional activation activity and Elongin BC binding activity and the functional domains of Elongin C having Elongin A activation activity and Elongin A and/or Elongin C binding activity have now been identified and isolated.		

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ELONGIN A AND C FUNCTIONAL DOMAINS

TECHNICAL FIELD OF THE INVENTION

5       The invention relates to the identification and characterization of the functional domains of the subunits of the elongation factor Elongin required for transcriptional activation of RNA Polymerase II and the regulation thereof.

## BACKGROUND OF THE INVENTION

Transcription is the synthesis of a strand of RNA representing or complementary to the coding strand of a DNA duplex. It takes place by the usual process of complementary base pairing and is catalyzed by the enzyme RNA polymerase. Transcription is the first step in the expression of a gene and it is the principle step at which gene expression is controlled or regulated.

The transcription process can be controlled at any one of the three stages of transcription: initiation, elongation, or termination. In eukaryotic systems, initiation involves the association of the RNA polymerase with several other enzymes and factors at the promoter. For accurate initiation, a number of the specific initiation factors are required.

Elongation is the phase in which the RNA polymerase moves along the strand of DNA, extending the growing RNA chain as it does so. As the RNA polymerase moves it unwinds the DNA helix to expose a new segment of the template in single-stranded form. Nucleotides are then covalently added to the 3' end of the elongating RNA chain forming an RNA-DNA hybrid in the unwound region. The DNA strand then re-associates with its DNA complement, thereby reforming the double helix structure and displacing the single-stranded RNA strand. Thus, elongation involves the transient disruption of DNA structure to form an unwound region that exists as a hybrid RNA-DNA duplex and a displaced single strand of DNA.

Termination of transcription occurs when the RNA polymerase reaches a termination codon, i.e., a noncoding segment of the DNA template strand. At this point, no additional nucleotides are added to the RNA chain. The termination stage ends when the RNA polymerase, DNA template, and newly synthesized RNA chain dissociate into separate entities.

Messenger RNA (mRNA) transcription is a complex bio-chemical process requiring the action of multiple transcription factors. Transcription factors include both initiation and elongation factors, which control the activity of the RNA polymerase at the initiation and elongation stages of transcription, respectively. Several of these factors are known to be essential for initiation and are referred to as factors D, E, A, G, and B from *Saccharomyces cerevisiae*,  $\tau$ ,  $\alpha$ ,  $\beta\gamma$ ,  $\delta$ , and  $\epsilon$  from rat liver, and TFIID, TFIIB, RAP30/74 or TFIIF, BTF2 or TFIIH, and TFIIE from human cells.

In addition to these factors, other proteins have been shown to stimulate either the initiation or elongation stages of transcription by RNA Polymerase II. One such factor, designated TFIIA, has been purified from both *Saccharomyces cerevisiae* and mammalian cells. TFIIA appears to promote assembly of the transcriptional pre-initiation complex. Although TFIIA is not essential for initiation, several lines of evidence suggest that it functions to increase the number of pre-initiation complexes that form at the promoter.

Considerable progress has recently been achieved identifying and characterizing transcriptional factors that support a basal level of transcription by RNA Polymerase II. Significantly less information, however, is available on transcription factors regulating the efficiency of transcriptional initiation or RNA chain elongation. Such transcriptional factors play an important role in regulating gene expression.

Currently, five general transcription elongation factors influencing RNA chain elongation have been identified and characterized with a high degree of certainty. These are SII, P-TEFb, TFIIF, ELL, and Elongin (also known as "SIII"). The general elongation factors TFIIF (RAP30/74) and ELL act to increase the overall rate of RNA chain elongation by suppressing transient pausing of the RNA polymerase at a variety of sites. The transcription factors SII and P-TEFb prevent RNA Polymerase II from arresting transcription prematurely. SII has been shown to promote RNA polymerase read-through at intrinsic pause sites in a human histone gene, the adenyl virus genome, and at several other sites. SII is a 38 kiloDalton (kD) elongation factor that promotes passage of RNA Polymerase II through transcriptional impediments such as nucleoprotein complexes and DNA sequences acting as intrinsic arrest sites. P-TEFb catalyzes the conversion of early, termination prone elongation complexes into productive elongation complexes.

A fifth elongation factor which increases the overall rate at which RNA Polymerase II transcribes DNA



is Elongin. Elongin is a trimeric complex consisting of three protein subunits labeled Elongin A (110 kD as measured by SDS-PAGE), Elongin B (18 kD as measured by SDS-PAGE), and Elongin C (15 kD as measured by SDS-PAGE) having 773, 118 and 112 amino acid residues, respectively. Elongin A is capable of weakly stimulating transcriptional activity at a low level in the absence of Elongin B and/or C, while Elongins B and C serve regulatory functions which increase the transcriptional activation activity of Elongin A. Elongins B and C bind stably to each other in the absence of Elongin A to form a binary complex (Elongin BC) that interacts with Elongin A strongly inducing its transcriptional activity.

In addition, it has been shown that Elongin C can assemble with Elongin A in the absence of Elongin B to form an Elongin AC complex which increased specific activity, thereby increasing the rate of RNA chain elongation. Elongin B does not interact with Elongin A in the absence of Elongin C and apparently functions like a chaperone protein facilitating the assembly and enhancing the stability of the Elongin ABC complex. The identification, purification and characterization of Elongin and its subunits Elongins A, B and C have been described in U.S. Serial No. 08/524,757 filed on September 7, 1995, and incorporated herein by reference.

Elongin has also been reported to interact with the product ("pVHL") of the Von Hippel-Lindau tumor suppressor gene. The Von Hippel-Lindau tumor

5 suppressor gene, which predisposes individuals to various tumor types, translates into a 213 amino acid protein capable of binding to and inhibiting the activity of Elongin. In particular, it has been reported that wild-type pVHL binds tightly and specifically to the Elongin BC complex and prevents it from activating Elongin A. That is, binding of the pVHL protein and Elongin A to the Elongin BC complex are mutually exclusive *in vitro*.

10 The previous work on Elongin described above provided a useful product for regulating the transcriptional activity of RNA Polymerase II. There still remained, however, a need to identify the functional domains of the Elongin subunits. As described herein, the Elongin A transcriptional activation domain has now been identified. This domain has been found to define a new evolutionarily conserved class of inducible activation domain. It has also been shown that the transcriptional activation domain of Elongin A and the Von Hippel-Lindau tumor suppressor protein (pVHL) interact with the Elongin BC complex through a conserved Elongin BC binding site motif essential for induction of Elongin A activity by Elongin BC and for tumor suppression by the VHL protein. In addition, the regions of Elongin C important for binding to Elongin B and for binding to and activating Elongin A have also been identified.

25 The identification and characterization of these domains serves two purposes. First, Elongin subunits or fragments thereof having at least the functional

30

domains described herein can be used in place of the entire subunits in *in vitro* transcriptional assays or systems. Secondly, and perhaps more importantly, these regions can be used as laboratory reagents for work  
5 concerning the transcriptional activation activities of Elongin.

## SUMMARY OF THE INVENTION

The present invention relates to the domains of Elongin A having transcriptional activation activity and Elongin BC binding activity. In another aspect, 5 the present invention relates to an analog of the human Elongin A.

In another aspect, the present invention relates to the domains of Elongin C having Elongin activation activity and Elongin A and/or Elongin B binding 10 activity.

In still another aspect, the present invention relates to the nucleotide sequences encoding the various Elongin subunits and their functional domains.

## BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1A. N- and C-terminal Elongin A deletion mutants analyzed in this study. At right, the results of assays described in the text and shown in panels 1C and 1D are summarized. N.D., not determined.

Fig. 1B. Wild type Elongin A was refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots of column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining. M, molecular weight markers; L, load; FT, flow through; kDa, kilodaltons; A, Elongin A; B, Elongin B; C, Elongin C.

Fig. 1C. N- and C-terminal Elongin A deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots containing ~100 ng of the peak column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining. In this and subsequent figures, WT designates wild type Elongin A.

Fig. 1D. Runoff transcription assays were performed as described. Reaction mixtures in lanes 1 and 10 contained no Elongin. Elongin complexes were present in reaction mixtures at the indicated relative molar concentrations; a relative molar concentration of 1 is equivalent to ~2 nM Elongin A. In this and subsequent figures, AdML indicates the position of the full-length ~250 nucleotide runoff transcript synthesized by RNA Polymerase II from the AdML promoter.

Fig. 2A. Analysis of Elongin A internal deletion mutants. At right, the results of assays described in the text and shown in panels 2B and 2C are summarized.

5 Fig. 2B. Elongin A internal deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots containing ~100 ng of the peak column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining.

10 Fig. 2C. Runoff transcription assays were performed as described. Elongin complexes were present in reaction mixtures at the indicated relative molar concentrations; a relative molar concentration of 1 is equivalent to ~2 nM Elongin A.

15 Fig. 3A. Analysis of short Elongin deletion mutants containing the minimal transcriptional activation domain. Elongin A deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots  
20 containing ~100 ng of the peak column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining.

Fig. 3B. Runoff transcription assays were performed as described. The reaction mixture in lane 1  
25 contained no Elongin. Elongin complexes were present in reaction mixtures at the indicated relative molar concentrations; a relative molar concentration of 1 is equivalent to ~2 nM.

Fig. 4A. Analysis of Elongin A internal deletion  
30 mutants with mutations in the potential Elongin BC

binding site. At the top is shown a comparison of the similar regions of Elongin A and the VHL protein. The portion of the VHL protein shown to be sufficient for binding to Elongin B and C (Kibel et al. 1995) is underlined; vertical lines indicate identical amino acids; colons indicate chemically similar amino acids. *EloA*, Elongin A; *VHL*, VHL protein.

Fig. 4B. Elongin A internal deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots containing ~100 ng of the peak column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining.

Fig. 5A. Transcription activity of Elongin A internal deletion and point mutants with mutations in the potential Elongin BC binding site. Runoff transcription assays were performed as described. Elongin complexes were present in reaction mixtures at the indicated relative molar concentrations; a relative molar concentration of 1 is equivalent to ~2 nM Elongin A.

Fig. 5B. Runoff transcription assays were performed as described in the absence and presence of excess wild type Elongin BC. Runoff transcription assays were performed in the presence of 4 nM TSK SP-NPR purified Elongin complexes of the indicated relative molar concentrations of purified Elongin BC complex; a relative molar concentration of 1 is equivalent to ~4 nM Elongin BC. BC, purified Elongin BC complex.

Fig. 6. Naturally occurring VHL mutants and synthetic Elongin A point mutants. EloA, Elongin A; VHL, VHL protein.

5 Fig. 7. Comparison of the amino acid sequences of rat and *C. elegans* Elongin A. Identical amino acids are shaded with black; chemically similar amino acids are shaded with gray. The Elongin BC binding site motif is boxed, and the region most highly conserved between rat and *C. elegans* Elongin A is underlined.

10 Fig. 8A. Analysis of wild type and mutant *C. elegans* Elongin A wherein wild type or mutant *C. elegans* Elongin A was refolded with rat Elongin B and C and subjected to TSK SP-NPR HPLC as described. Aliquots of the peak column fractions were analyzed by  
15 SDS-PAGE, and proteins were visualized by silver staining. WT *C.e.* EloA, wild type *C. elegans* Elongin A (SEQ ID NO:42); 202-434, *C. elegans* Elongin A mutant containing residues 202-434 (SEQ ID NO:45).

20 Fig. 8B. ~2 pmol of human or *C. elegans* Elongin A proteins were refolded as described (Bradslier et al. 1993a) in the presence or absence of ~2 pmol of rat Elongin B and C. Aliquots of refolded protein were assayed for transcriptional activity in oligo dc-tailed  
25 mixtures contained no Elongin (lane 1); 3 and 9  $\mu$ l of renatured human Elongin A without (lanes 2 and 3) or with (lanes 4 and 5) Elongin B and C; 3 and 9  $\mu$ l of renatured wild type *C. elegans* Elongin A without (lanes 6 and 7) or with (lanes 8 and 9) Elongin B and C; 3 and  
30 9  $\mu$ l of renatured *C.e.* EloA(94-434) (SEQ ID NO:44)



without (lanes 10 and 11) or with (lanes 12 and 13) Elongin B and C; 3 and 9  $\mu$ l of renatured C.e. EloA (202-434) (SEQ ID NO:45) with (lanes 14 and 15) or without (lanes 16, and 17) Elongin B and C.

5           Fig. 9. Elongin C mutants analyzed in this study.

          Fig. 10A. Assay of formation of Elongin BC complexes containing wild type and mutant Elongin C wherein wild type Elongin B (upper panel), wild type Elongin C (middle panel), or a mixture of wild type  
10 Elongin B and C were refolded and subjected to DEAE-NPR HPLC as described. Aliquots of the indicated column fractions were analyzed by SDS-PAGE, and proteins were visualized by silver staining.

          Fig. 10B. N-terminal, C-terminal, and internal  
15 Elongin C deletion mutants were assayed for their abilities to form Elongin BC complexes as described.

          Fig. 10C. Elongin C alanine scanning mutants were assayed for their abilities to form Elongin BC complexes as described. C(Ala19-21) (SEQ ID NO:61) co-electrophoreses with wild type Elongin B during SDS-  
20 PAGE. B, Elongin B; C, wild type or mutant Elongin C; L, load; FT, flow-through.

          FIG. 11A. Assay of activation of Elongin A by wild type and mutant Elongin BC complexes wherein  
25 runoff transcription assays were performed as described according the protocol diagramed at the bottom of the figure. A mixture containing ~50 ng of SP-NPR purified Elongin A and ~5 ng (1x BC) or ~50 ng (10x BC) of purified wild type or mutant Elongin BC was  
30 preincubated on ice for 60 min prior to addition to

reaction mixtures. Purified Elongin BC complexes were from the following DEAE-NPR fractions shown in Fig.

10B: Wild type (SEQ ID NO:9), fraction 7; BC(15-112) (SEQ ID NO:46), fraction 5; BC(19-112) (SEQ ID NO:47),  
5 fraction 5; BC(1-97) (SEQ ID NO:51), fraction 6; and BC(1-83) (SEQ ID NO:52), fraction 5. Reactions shown in lanes 1 and 7 contained no Elongin BC. WT, wild type.

Fig. 11B. Runoff transcription assays were performed as described in the legend to Fig. 11A with  
10 Elongin BC complexes from the following DEAE-NPR fractions shown in Fig. 10B: wild type (SEQ ID NO:9), fraction 7, BC( $\Delta$ 31-40) (SEQ ID NO:54), fraction 6; BC( $\Delta$ 41-50) (SEQ ID NO:55), fraction 7; BC( $\Delta$ 51-60) (SEQ ID NO:56), fraction 5; BC( $\Delta$ 61-70) (SEQ ID NO:57),  
15 fraction 13; BC( $\Delta$ 71-80) (SEQ ID NO:58), fraction 7; BC( $\Delta$ 81-90) (SEQ ID NO:59), fraction 7; BC( $\Delta$ 91-100) (SEQ ID NO:60), fraction 6. Runoff transcription is expressed in arbitrary units normalized to the amount of product synthesized in the presence of 1X (white  
20 boxes) or 10X (black boxes) wild type Elongin BC.

Fig. 12A. Assay of activation of Elongin A by Elongin C mutants that do not form isolable Elongin BC complexes. Runoff transcription assays were performed as described according to the protocol diagramed at the  
25 bottom of Fig. 11A. A mixture containing ~50 ng of SP-NPR purified Elongin A and ~5 ng (1xC) or ~50 ng (10xC) of Ni<sup>2+</sup>-purified and refolded wild type or mutant Elongin C was preincubated on ice for 60 min and then added to reaction mixtures at -10°C.

Fig. 12B. Assay of activation of Elongin A by C(Ala19-21) (SEQ ID NO:61) and C(Ala22-24) (SEQ ID NO:62). Runoff transcription assays were performed as described in the legend to Fig. 11A with Elongin BC complexes from the following DEAE-NPR fractions shown in Fig. 10C: wild type BC, fraction 7; BC(Ala19-21) (SEQ ID NO:61), fraction 7; BC(Ala22-24) (SEQ ID NO:62), fraction 7. Runoff transcription is expressed in arbitrary units normalized to the amount of product synthesized in the presence of 1X (white boxes) or 10X (black boxes) wild type Elongin BC.

Fig. 13. Assay of formation of Elongin ABC complexes containing N-terminal and C-terminal Elongin C mutants. Mixtures containing wild type Elongin A and B and wild type or mutant Elongin C were refolded and subjected to SP-NPR HPLC as described. Aliquots of peak fractions from isolation of Elongin ABC complexes were analyzed by SDS-PAGE, and proteins were visualized by silver staining. A, Elongin A; B, Elongin B; C, wild type or mutant Elongin C.

Fig. 14A. Assay of formation and activity of Elongin ABC complexes containing Elongin C internal deletion mutants wherein formation of Elongin ABC complexes was assayed as described in the legend to Fig. 13.

Fig. 14B. Runoff transcription assays were performed as described according to the protocol diagramed at the bottom of Fig. 11A. Isolated Elongin ABC complexes were added to reactions at -10'. A, Elongin A; B, Elongin B; C, Elongin C.

Fig. 15. Assay of activation of Elongin A by isolated BC complexes containing Elongin C C-terminal alanine scanning mutants. Runoff transcription assays were performed as described in the legend to Fig. 11A. Runoff transcription is expressed in arbitrary units normalized to the amount of product synthesized in the presence of 1X (white boxes) or 10X (black boxes) wild type Elongin BC.

Fig. 16. Summary of Elongin C mutations that most strongly affect the ability of Elongin C to bind to Elongin B (B binding), to bind to Elongin A (A binding), and to activate Elongin A (Activation of Elongin A). Mutations in the region indicated by the open box strongly affect activation of Elongin A by isolated Elongin BC complexes but not of isolated Elongin ABC complexes. HZ, hydrophobic zipper.

**DETAILED DESCRIPTION**

The present invention relates to the Elongin A domains required for transcriptional elongation activation and for binding to Elongin BC and of the Elongin C domains required for interaction with Elongin B and activation of Elongin A's transcriptional elongation activity and the use of these domains.

**Elongin A**

Wild-type Elongin A is a 773 amino acid protein (SEQ ID NO:1) which stimulates the elongation activity of RNA Polymerase II. Fragments of the wild-type Elongin A having amino acid residues 1 to 730 (SEQ ID NO:2), 1 to 680 (SEQ ID NO:3), and 400-773 (SEQ ID NO:4) each possess about 50% or more of the elongation activation activity exhibited by wild-type Elongin A. From the results it can be predicted that fragments of the wild-type Elongin A having amino acid residues 400-730 (SEQ ID NO:5) and 400-680 (SEQ ID NO:6) will also possess about 50% or more of the elongation activity exhibited by wild-type Elongin A.

The Elongin A sequence critical for binding to Elongins B and C also falls within this 374 amino acid sequence, i.e., between residues 400 and 773 (SEQ ID NO:4). This sequence, i.e., the Elongin B and C binding region of Elongin A, falls within a 20 amino acid region between residues 546 and 565 (SEQ ID NO:7) and preferably within a 12 amino acid region between residues 549 and 560 (SEQ ID NO:8).

Thus, the Elongin A region encompassing amino acid residues 400-773 (SEQ ID NO:4) includes all of the sequences necessary for full Elongin A transcriptional elongation activity and for regulation by Elongin BC.

5 An Elongin A protein or fragment thereof containing this entire wild-type 374 amino acid region or a substantial portion of it will exhibit significant elongation activation activity and can be used in a variety of *in vitro* transcription systems or assays by

10 one of ordinary skill in the art.

#### Elongin C

Wild-type Elongin C is a 112 amino acid protein (SEQ ID NO:9) which induces the transcriptional activity of Elongin A. The regions of the wild-type

15 Elongin C required for (1) binding to Elongin B, (2) binding to Elongin A, and (3) activation of Elongin A transcriptional activity have now been localized. These regions are the amino acids between (1) residues 19 and 30 (SEQ ID NO:10), (2) residues 19 and 30 (SEQ

20 ID NO:10) and 100 and 112 (SEQ ID NO:11), and (3) residues 19 and 30 (SEQ ID NO:10), 60 and 71 (SEQ ID NO:12) and 91-112 (SEQ ID NO:13), respectively.

Thus, an Elongin C protein or fragment thereof containing these wild-type regions will possess all

25 sequences necessary for interaction and binding with Elongins A and B and can be used in a variety of *in vitro* transcription systems or assays by one of ordinary skill in the art.

Construction of the Elongin A and C subunits as well as N- and C- terminal and internal deletion mutants thereof was done as described in Examples 2 and 13. Expression and purification of these subunits was done as described in Examples 2, 3 and 14.

Identification and Characterization of the Elongin A Domains Required for Transcriptional Activation and Binding to Elongin BC

Elongin A is a 773 amino acid protein (SEQ ID NO:1) with a calculated molecular mass of 87.2 kDa as calculated from the amino acid sequence predicted from the cDNA. It has now been determined that an Elongin A region encompassing amino acids 400-773 (SEQ ID NO:4) includes all sequences necessary for full Elongin A transcriptional activity and for regulation by Elongin BC. The most critical sequences within the Elongin A transcriptional activation domain (residues 400-773) (SEQ ID NO:4) have been localized to an ~171 amino acid region between residues 520 and 690 (SEQ ID NO:14). Sequences outside this region, though not essential for activation of transcription, either participate in interactions with the RNA Polymerase II elongation complex or help to maintain the structural integrity of the transcriptional activation domain. Finally, the transcriptional activation domain of Elongin A has been found to be evolutionarily conserved in species as distantly related as *C. elongans* (nematode) and man.

It has also been determined that the Elongin A sequence critical for binding to Elongin B and C fall

within a 19 amino acid region between residues 546 and 565 (SEQ ID NO:7) and preferably within a 12 amino acid region between residues 549 and 560 (SEQ ID NO:8).

This region shares a sequence similarity with a short  
5 region of the VHL protein (residues 157-172) (SEQ ID NO:15) previously shown to be sufficient for binding to Elongin B and C (Kibel, 1995). Within this conserved Elongin BC binding site motif (consensus sequence TLx3Cx2V[V,2]) SEQ ID NO:16 identical threonine,  
10 leucine, cysteine and valine are found in Elongin A and VHL at the positions designated 1, 2, 6 and 9 in SEQ ID NO:8 for Elongin A and in SEQ ID NO:15 for VHL protein.

Localization of the Elongin A Transcriptional Activation Domain

15 The Elongin A transcriptional activation domain was located and the Elongin BC binding site was identified using a series of N- and C-terminal Elongin A deletion mutants (Fig. 1A). These Elongin A deletion mutants were constructed, expressed in *E. coli*,  
20 purified, and assayed for their abilities (i) to assemble into chromatographically isolable Elongin ABC complexes and (ii) to stimulate the rate of elongation of transcripts synthesized by RNA Polymerase II from the AdML promoter in a reconstituted basal  
25 transcription system composed of TBP and the general initiation factors TFIIB, TFIIE, TFIIIF, and TFIIH.

To test the abilities of Elongin A mutants to bind Elongin B and C and to isolate mutant Elongin ABC complexes for assay of their relative transcriptional



activities, N- and C-terminal Elongin A deletion mutants were refolded together with wild type Elongin B and C and subjected to TSK SP-NPR HPLC. Both wild type and mutant Elongin ABC complexes bind tightly to TSK SP-NPR and elute at salt concentrations between 0.2 and 0.4 M KCl, whereas excess Elongin B and C flow through this resin at 0.1 M KCl (Aso et al. 1995b). Fig. 1B shows SDS-PAGE analysis of aliquots of column fractions from TSK SP-NPR HPLC purification of wild type Elongin ABC complexes. Fig. 1C shows SDS-PAGE analysis of aliquots of peak column fractions from TSK SP-NPR HPLC purification of mutant Elongin ABC complexes: wild type (WT) (SEQ ID NO:1); 400-773 (SEQ ID NO:4); 1-730 (SEQ ID NO:2); 1-680 (SEQ ID NO:3); 1-630 (SEQ ID NO:17); and 1-535 (SEQ ID NO:18). Results of this analysis revealed that all N- and C-terminal Elongin A deletion mutants except A(1-535) (SEQ ID NO:18), which lacks the region similar to the Elongin BC binding site in the VHL protein (Kibel et al. 1995), were able to bind stably to Elongin B and C to form isolable Elongin ABC complexes.

The relative transcriptional activation activities of the wild type and mutant Elongin ABC complexes shown in Fig. 1C were then compared in runoff transcription assays. Preinitiation complexes were assembled at the AdML promoter, wild type and mutant Elongin ABC complexes were added to reaction mixtures, and transcription was initiated by addition of limiting concentrations of ribonucleoside triphosphates. Under these conditions, the rate of RNA chain elongation is

very slow, and runoff transcripts do not accumulate unless elongation stimulatory activity is present. Bradsher et al. 1993b; Aso et al. 1995b. Fig. 1D, lanes 1 and 2.

5        Results of these experiments indicated that the first 400 Elongin A amino acids (SEQ ID NO:19) (which include a region of SII similarity and a potential ATP binding site), are dispensable for Elongin ABC activity in vitro, since deletion of this region had no  
10        significant effect on accumulation of runoff transcripts. In contrast, deletion of the C terminal 93 amino acids (SEQ ID NO:3), which includes a potential hydrophobic zipper, decreased Elongin ABC activity by approximately 50%, and deletion of the C-  
15        terminal 143 amino acids (SEQ ID NO:17) abolished detectable Elongin ABC activity. Taken together, these results identified (i) a 20 amino acid Elongin A region (residues 546 to 565) (SEQ ID NO:7), which includes sequences required for interaction with Elongin B and  
20        C, (ii) a 281 amino acid Elongin A region (residues 400 to 680) (SEQ ID NO:6), which includes sequences required for transcriptional activity, and (iii) an additional C-terminal Elongin A region (residues 680 to 773) (SEQ ID NO:20), which includes sequences important  
25        for maximal transcriptional activity.

      The Elongin A sequences required for binding to Elongin B and C and for transcriptional activity were further defined using a series of Elongin A internal deletion mutants. These mutants (Fig. 2A), with  
30        mutations spanning the transcriptional activation

domain from residues 400 to 730 (SEQ ID NO:5) were constructed, expressed in *E. coli*, purified, and assayed as described above. The mutant sequences tested were:  $\Delta$ 401-440 (SEQ ID NO:21);  $\Delta$ 441-480 (SEQ ID NO:22);  $\Delta$ 481-520 (SEQ ID NO:23);  $\Delta$ 521-545 (SEQ ID NO:24);  $\Delta$ 546-565 (SEQ ID NO:25);  $\Delta$ 566-585 (SEQ ID NO:26);  $\Delta$ 586-610 (SEQ ID NO:27);  $\Delta$ 611-650 (SEQ ID NO:28);  $\Delta$ 651-690 (SEQ ID NO:29); and  $\Delta$ 691-730 (SEQ ID NO:30).

All Elongin A internal deletion mutants, except  $\Delta$ 546-565 (SEQ ID NO:25), which lacks the region similar to the Elongin BC binding site found in the VHL protein (Kibel et al. 1995), were capable of binding to Elongin B and C (Figs. 2A and 2B). As shown in Fig. 2C, Elongin ABC complexes containing Elongin A internal deletion mutants  $\Delta$ 401-440 (SEQ ID NO:21),  $\Delta$ 441-480 (SEQ ID NO:22),  $\Delta$ 481-520 (SEQ ID NO:23), and  $\Delta$ 691-730 (SEQ ID NO:30) exhibited significant transcriptional activity. In contrast, Elongin ABC complexes containing Elongin A internal deletion mutants lacking sequences located in the region between amino acids 520 and 691 were profoundly impaired in their abilities to stimulate elongation by RNA Polymerase II.

Notably, the Elongin ABC complex containing Elongin A internal deletion mutant  $\Delta$ 521-545 (SEQ ID NO:24), which lacks a potential topoisomerase I catalytic site motif, is inactive in activating transcription. Topoisomerase I activity is unlikely to play a role in Elongin (SIII) function *in vitro*, however, because (i) we observed that mutating the

potential active site tyrosine at residue 543 to either phenylalanine or serine had no effect on Elongin A transcriptional activation activity (data not shown) and (ii) we have been unable to detect topoisomerase I activity associated with Elongin A

Taken together, analysis of the N-terminal, C-terminal, and internal Elongin A deletion mutants localized sequences critical for transcriptional activity to a minimal region of ~170 amino acids between residues 521 and 690 (SEQ ID NO:31). Further investigation revealed, however, that Elongin A sequences outside this minimal region also make significant contributions to the transcriptional activation activity of Elongin A. For example, Elongin A mutants composed of residues 500 to 730 (SEQ ID NO:32) or residues 500 to 700 (SEQ ID NO:33) were transcriptionally inactive, even though they assembled into isolable Elongin ABC complexes (Fig. 3). Thus, Elongin A sequences outside the minimal transcriptional activation domain make secondary contributions to Elongin activity, either by participating directly in interactions with the RNA Polymerase II elongation complex or by helping to maintain the proper three dimensional structure of the transcriptional activation domain.

#### Identification of the Elongin BC Binding Site

Analysis of Elongin A deletion mutants revealed that the Elongin A region between residues 546 and 565 (SEQ ID NO:7) plays an important role in binding to

Elongin B and C. As shown in Fig. 4A, this Elongin A region shares sequence similarity with a short region of the VHL protein (residues 157-172, underlined) (SEQ ID NO:15) previously shown to be sufficient for binding to Elongin B and C (Kibel et al. 1995). This Elongin A region was further defined using a systematic series of Elongin A internal deletion mutants spanning residues 545 to 568 (SEQ ID NO:34). These mutants (Fig. 4A) were constructed, expressed in *E. coli*, purified, and assayed for their abilities to assemble into chromatographically isolable Elongin ABC complexes and to stimulate the rate of elongation by RNA Polymerase II. The mutants tested were:  $\Delta$ 545-548 (SEQ ID NO:35);  $\Delta$ 549-552 (SEQ ID NO:36);  $\Delta$ 553-556 (SEQ ID NO:37);  $\Delta$ 557-560 (SEQ ID NO:38);  $\Delta$ 561-564 (SEQ ID NO:39); and  $\Delta$ 565-568 (SEQ ID NO:40).

As shown in Fig 4B, Elongin A internal deletion mutants  $\Delta$ 545-548 (SEQ ID NO:35),  $\Delta$ 561-564 (SEQ ID NO:39), and  $\Delta$ 565-568 (SEQ ID NO:40) bound stably to Elongin B and C to form Elongin ABC complexes that could be purified by TSK SP-NPR HPLC. In contrast, Elongin A internal deletion mutants  $\Delta$ 549-552 (SEQ ID NO:36),  $\Delta$ 553-556 (SEQ ID NO:37), and  $\Delta$ 557-560 (SEQ ID NO:38), each of which lack Elongin A sequences within the region most similar to the Elongin BC binding site of the VHL protein, were impaired in their abilities to bind to Elongin B and C.

To assess the transcriptional activities of the Elongin A internal deletion mutants, aliquots of peak fractions shown in Fig. 4B from TSK SP-NPR HPLC

purification of mutant Elongin ABC complexes were assayed for their abilities to stimulate the rate of elongation by RNA Polymerase II. Because they co-purified with variable amounts of Elongin B and C, these mutants were assayed in the absence (Fig. 5A) and presence (Fig. 5B) of excess purified Elongin BC complex.

The results of these assays revealed that all Elongin A deletion mutants with mutations between amino acid residues 545 and 568 were transcriptionally impaired, although not all mutants were impaired to the same extent. Two Elongin A deletion mutants,  $\Delta$ 545-548 (SEQ ID NO:35) and  $\Delta$ 565-568 (SEQ ID NO:40), which efficiently formed isolable Elongin ABC complexes, exhibited reduced but readily detectable transcriptional activity, whereas Elongin A mutant  $\Delta$ 561-564 (SEQ ID NO:39), which could also bind Elongin B and C, exhibited little activity. In addition, two Elongin A deletion mutants,  $\Delta$ 549-552 (SEQ ID NO:36) and  $\Delta$ 553-556 (SEQ ID NO:37), which were severely impaired in their abilities to form isolable Elongin ABC complexes, exhibited little or no detectable transcriptional activity, whereas Elongin A mutant  $\Delta$ 557-560 (SEQ ID NO:38), which was also impaired in its ability to form an isolable Elongin ABC complex, exhibited detectable activity, raising the possibility that deletion of Elongin A residues between 556 to 561 (SEQ ID NO:41) may result in an increase in the basal activity of Elongin A.

The results described above indicate that Elongin A sequences most critical for binding to Elongin B and C fall within a 12 amino acid region between residues 549 and 560 (SEQ ID NO:8). Both Elongin A (SEQ ID NO:8) and the VHL protein (SEQ ID NO:15) share conserved threonine, leucine, cysteine, and valine residues in their Elongin BC binding region at the positions designated 1, 2, 6, and 9 in Fig. 6. The importance of these residues is further underscored by investigations of mutations found in VHL families and in clear-cell renal carcinoma which have identified naturally occurring VHL point mutations of the conserved threonine, leucine, and cysteine residues, but not of the conserved valine residue (Latif et al. 1993; Gnarra et al. 1994; Chen et al. 1995; Kanno et al. 1994; Whaley et al. 1994; Foster et al. 1994).

To investigate the importance of these residues for Elongin A transcriptional activation activity, Elongin A mutants carrying point mutations of the conserved threonine, leucine, cysteine, and valine residues were constructed, expressed in *E. coli*, purified, and assayed for their abilities to form isolable Elongin ABC complexes and to stimulate the rate of elongation by RNA Polymerase II. As shown in Fig. 4B, each of the Elongin A point mutants, except L550S, formed readily detectable Elongin ABC complexes that could be purified by TSK SP-NPR HPLC, although Elongin A mutants T549I and C554F appeared somewhat impaired in their abilities to form Elongin ABC complexes.

To assess the transcriptional activities of the Elongin A point mutants, aliquots of peak fractions shown in Fig. 4B were assayed for their abilities to stimulate the rate of elongation by RNA Polymerase II in the absence (Fig. 5A) and presence (Fig. 5B) of excess purified Elongin BC complex. Only Elongin A point mutant V557E, which is mutated at a position where there are no corresponding naturally occurring VHL mutations, exhibited near wild type activity.

10 Evolutionary Conservation of the Elongin A  
Transcriptional Activation Domain

A TBLASTN search of the GenBank non-redundant database using rat Elongin A as the query sequence identified a predicted *C. elegans* ORF encoding a potential Elongin A homolog. By screening a *C. elegans* cDNA library with a probe derived from the predicted ORF, we isolated a cDNA encoding a highly basic, 434 amino acid protein (SEQ ID NO:42) with a calculated molecular mass of 49.2 kDa. Comparison of the predicted amino acid sequences of mammalian Elongin A and the potential *C. elegans* Elongin A homolog revealed two conserved regions: an N-terminal region resembling the SII-like N-terminus of mammalian Elongin A and a C-terminal region resembling the C-terminal transcriptional activation domain of mammalian Elongin A. Notably, the potential *C. elegans* Elongin A homolog exhibited the greatest similarity (33% identity, 53% similarity, alignment score 17.8 SD) to mammalian Elongin A residues 520 to 662 (SEQ ID NO:43), which



includes the majority of the region most critical for transcriptional activity (Fig. 7). In addition, this region of the *C. elegans* protein includes a short sequence that resembles the Elongin BC binding site found in the VHL protein; however, it lacks the topoisomerase I catalytic site motif.

To determine the functional relationship between mammalian Elongin A and the potential *C. elegans* Elongin A homolog, the intact *C. elegans* ORF and two N-terminal deletion mutants C.e.EloA(94-434) (SEQ ID NO:44) and C.e.EloA(202-434) (SEQ ID NO:45) were constructed, expressed in *E. coli*, purified, and assayed for their abilities to interact with mammalian Elongin B and C and to stimulate the rate of elongation by mammalian RNA Polymerase II. Mutant C.e.EloA(94-434) (SEQ ID NO:44) lacks sequences related to SII, but contains sequences similar to the Elongin A transcriptional activation and Elongin BC binding site. Mutant C.e.EloA contains the potential Elongin BC binding site, but lacks sequences similar to the N-terminus of the transcriptional activation domain of mammalian Elongin A.

Both the full-length *C. elegans* protein (SEQ ID NO:42) and mutants C.e.EloA(94-434) (SEQ ID NO:44) and C.e.EloA(202-434) (SEQ ID NO:45) were capable of binding to mammalian Elongin B and C (Fig. 8A and data not shown). In addition, the full-length *C. elegans* protein (SEQ ID NO:42) was capable of stimulating the rate of elongation by mammalian RNA Polymerase II in a reaction dependent on mammalian Elongin B and C (Fig.

8B). In these experiments, the transcriptional activities of mammalian Elongin A and the *C. elegans* protein were compared using an oligo(dC)-tailed template assay (Kadesch and Chamberlin, 1982; Tan et al. 1994a), which permits direct measurement of the effect of elongation factors on the rate of RNA chain elongation by RNA Polymerase II in the absence of initiation factors. Consistent with our results from analysis of mammalian Elongin A, mutant C.e.EloA(94-434) (SEQ ID NO:44), which contains the entire Elongin A-like transcriptional activation domain, was as active as the wild type *C. elegans* protein in stimulating the rate of elongation by mammalian RNA Polymerase II, whereas mutant C.e.EloA(202-434) (SEQ ID NO:45), which lacks the N-terminus of the Elongin A-like transcriptional activation domain, had significantly reduced activity.

Identification and Characterization of the Elongin C Domains Required for Interaction with Elongin B and Activation of Elongin A

Elongin C is a 112 amino acid protein (SEQ ID NO:9) with a calculated mass of 12.4 kD as calculated from the amino acid sequence predicted from the cDNA. Elongin C is a regulatory subunit of the Elongin ABC which (i) functions as a potent stimulator of Elongin A transcriptional activation activity, (ii) interacts specifically with Elongin B to form an isolable Elongin BC complex, and (iii) is bound and negatively regulated *in vitro* by the product of the von Hippel-Lindau (VHL) tumor suppressor gene. As described herein, the

Elongin C regions important for binding to Elongin B and for binding to and activating of Elongin A have now been localized.

Identification of an Elongin C Region Important for Binding to Elongin B

5

The regions of Elongin C which interact with Elongin B were localized using a systematic series of N-terminal, C-terminal, and internal Elongin C deletion mutants. These mutants (Fig. 9) were constructed, expressed in E. coli, purified, and assayed for their abilities to form chromatographically isolable Elongin BC complexes. The mutants tested were: 15-112 (SEQ ID NO:46); 19-112 (SEQ ID NO:47); 23-112 (SEQ ID NO:48); 29-112 (SEQ ID NO:49); 57-112 (SEQ ID NO:50); 1-97 (SEQ ID NO:51); 1-83 (SEQ ID NO:52);  $\Delta$ 21-30 (SEQ ID NO:53);  $\Delta$ 31-40 (SEQ ID NO:54);  $\Delta$ 41-50 (SEQ ID NO:55);  $\Delta$ 51-60 (SEQ ID NO:56);  $\Delta$ 61-70 (SEQ ID NO:57);  $\Delta$ 71-80 (SEQ ID NO:58);  $\Delta$ 81-90 (SEQ ID NO:59);  $\Delta$ 91-100 (SEQ ID NO:60); Ala19-21 (SEQ ID NO:61); Ala22-24 (SEQ ID NO:62); Ala25-27 (SEQ ID NO:63); Ala28-30 (SEQ ID NO:64); Ala89-91 (SEQ ID NO:65); Ala92-94 (SEQ ID NO:66); Ala95-97 (SEQ ID NO:67); Ala98-100 (SEQ ID NO:68); Ala101-103 (SEQ ID NO:69); Ala104-106 (SEQ ID NO:70); Ala107-109 (SEQ ID NO:71); and Ala110-112 (SEQ ID NO:72).

In these experiments, individual Elongin C mutants were refolded together with wild type Elongin B and subjected to TSK DEAE-NPR HPLC. The Elongin BC complex elutes from TSK DEAE-NPR as a discrete species with

chromatographic properties distinct from those of both wild type Elongin B, which flows through TSK DEAE-NPR at low ionic strength, and wild type Elongin C, which binds tighter to this resin than the Elongin BC complex (Fig 10A). As shown in Fig. 10B, deletion of as many as 29 amino acids from the C-terminus of Elongin C (SEQ ID NO:52) had no detectable effect on formation of isolable Elongin BC complexes. Likewise, deletion of as many as 18 amino acids from the N-terminus of Elongin C (SEQ ID NO:47) had no detectable effect on formation of isolable Elongin BC complexes.

Deletion of 22 amino acids (SEQ ID NO:48) from the N-terminus of Elongin C, however, abolished formation of isolable Elongin BC complexes. This suggests that Elongin C residues between 18 and 22 (SEQ ID NO:73) are critical for interaction of Elongin B and C. Consistent with this possibility, an Elongin C internal deletion mutant lacking residues 21 to 30 (SEQ ID NO:53) did not form an isolable Elongin BC complex (Fig. 10B). Notably, this mutant was the only Elongin C internal deletion mutant that failed to bind to Elongin B, suggesting that the Elongin C region between residues 18 and 30 (SEQ ID NO:74) either contains the Elongin B binding site or is crucial for proper folding of the protein.

Further evidence supporting the importance of Elongin C sequences within this region, i.e., residues 18 to 30 (SEQ ID NO:74), for binding to Elongin B came from analysis of a set of clustered alanine scanning mutants in which Elongin C residues between amino acids

19 and 30 (SEQ ID NO:10) were mutated three at a time to alanines. As shown in Fig. 10C, although Elongin C alanine scanning mutants C(Ala19-21) (SEQ ID NO:61) and C(Ala22-24) (SEQ ID NO:62) were capable of assembling into isolable Elongin BC complexes, C(Ala25-27) (SEQ ID NO:63) and C(Ala28-30) (SEQ ID NO:64) were not.

Characterization of Elongin C Regions Important for Activation of Elongin A

Pre-assembled Elongin BC complexes are capable of activating Elongin A. To investigate the requirements for activation of Elongin A by Elongin C, the isolated wild type and mutant Elongin BC complexes shown in Fig. 10A and Fig. 10B were assayed for their abilities to stimulate the rate of accumulation of runoff transcripts synthesized by RNA Polymerase II from the AdML promoter in a reconstituted transcription system containing purified Elongin A and the general initiation factors TBP, TFIIB, TFIIE, TFIIIF, and TFIIH. As shown in Figs. 11A and 11B, the entire C-terminal half of Elongin C is critical for activation of Elongin A by pre-assembled Elongin BC complexes. Elongin BC complexes containing Elongin C deletion mutants lacking up to 18 amino acids from their N-termini (SEQ ID NO:46; SEQ ID NO:47) or sequences between amino acids 41 and 60 (SEQ ID NO:55; SEQ ID NO:56) were capable of activating Elongin A. Elongin BC complexes containing Elongin C deletion mutants lacking as few as 15 amino acids from their C-terminal (SEQ ID NO:51) were inactive. (Fig. 11A) Furthermore, Elongin BC

complexes containing Elongin C internal deletion mutants lacking sequences C-terminal to amino acid 61 (SEQ ID NO:57; SEQ ID NO:58; SEQ ID NO:59; SEQ ID NO:60) were inactive, and an Elongin BC complex  
5 containing the internal deletion mutant CA31-40 (SEQ ID NO:54), which lacks sequences immediately C-terminal to the region important for Elongin B binding, was also inactive.

Although Elongin B facilitates assembly and  
10 enhances stability of the Elongin ABC complex, it is not essential for activation of Elongin A by Elongin C. As described above, Elongin C mutants containing mutations in the region between amino acids 19 and 30 (SEQ ID NO:10) were unable to form isolable Elongin BC  
15 complexes. To investigate the ability of these Elongin C mutants to activate Elongin A, they were assayed for their abilities to stimulate the rate of accumulation of runoff transcripts synthesized by RNA Polymerase II from the AdML promoter in the presence of Elongin A and  
20 the general initiation factors, but in the absence of Elongin B. As shown in Fig. 12A, although wild type Elongin C strongly activated Elongin A, none of the Elongin C mutants containing mutations between amino acids 19 and 30 (SEQ ID NO:10), except alanine scanning  
25 mutant C(Ala22-24) (SEQ ID NO:62) (Fig. 12B), was capable of activating Elongin A. Thus, the Elongin C region between amino acids 19 and 30 (SEQ ID NO:10) is important for both Elongin B binding and activation of Elongin A.

To investigate whether Elongin C deletion mutants that fail to activate Elongin A are defective in their abilities to bind Elongin A, the Elongin C deletion mutants were assayed for their abilities to form chromatographically isolable Elongin ABC complexes. In these experiments, individual Elongin C deletion mutants were refolded together with wild type Elongin A and B and subjected to TSK SP-NPR HPLC. As described previously, Elongin A, Elongin AC and Elongin ABC complexes bind tightly to TSK SP-NPR and can all be eluted with ~0.3 M KCl, whereas Elongin B and C flow through this resin at low ionic strength.

As shown in Fig. 13, the N-terminal Elongin C deletion mutant C(15-112) (SEQ ID NO:46) and C(19-112) (SEQ ID NO:47), which form isolable Elongin BC complexes that activate Elongin A, were capable of assembling into isolable Elongin ABC complexes, whereas the remaining N-terminal and C-terminal Elongin C deletion mutants (C(23-112) (SEQ ID NO:48); C(29-112) (SEQ ID NO:49); C(57-112) (SEQ ID NO:50); C(1-97) (SEQ ID NO:51); and C(1-83) (SEQ ID NO:52)), each of which form inactive Elongin BC complexes, were unable to form isolable Elongin ABC complexes.

In contrast, with the exception of Elongin C internal deletion mutant, C( $\Delta$ 21-30) (SEQ ID NO:53), which lacks residues 21 to 30 and does not form an isolable Elongin BC complex, each of the Elongin C internal deletion mutants (C( $\Delta$ 31-40) (SEQ ID NO:54); C( $\Delta$ 41-50) (SEQ ID NO:55); C( $\Delta$ 51-60) (SEQ ID NO:56); C( $\Delta$ 61-70) (SEQ ID NO:57); C( $\Delta$ 71-80) (SEQ ID NO:58);

C( $\Delta$ 81-90) (SEQ ID NO:59); C( $\Delta$ 91-100) (SEQ ID NO:60))  
was capable of forming an isolable Elongin ABC complex  
(Fig. 14A). In these experiments, the yield of Elongin  
B and C in purified Elongin ABC complexes containing  
5 Elongin C internal deletion mutants was routinely less  
than their yield in purified Elongin ABC complexes  
containing wild type Elongin C, suggesting that Elongin  
ABC complexes containing the internal deletion mutants  
assemble less efficiently or are less stable than wild  
10 type Elongin ABC complexes.

Runoff transcription assays were used to compare  
the activities of the isolated wild type and mutant  
Elongin ABC complexes shown in Fig. 14A. The  
concentration of the wild type Elongin ABC complex in  
15 the reaction shown in lane 2 of Fig. 14B was sufficient  
to saturate the assay, and the concentrations of mutant  
Elongin ABC complexes were adjusted so that all  
reactions shown in Fig. 14B contained equivalent levels  
of Elongin A. Results of transcription assays  
20 highlighted the importance of sequences at the C-  
terminus of Elongin C for activation of Elongin A.  
Elongin ABC complexes containing Elongin C mutants  $\Delta$ 91-  
100 (SEQ ID NO:60),  $\Delta$ 61-70 (SEQ ID NO:57), and  $\Delta$ 21-30  
(SEQ ID NO:53) were unable to stimulate the rate of  
25 elongation by RNA Polymerase II.

In addition, although Elongin BC complexes  
containing Elongin C internal deletion mutants C( $\Delta$ 71-  
80) (SEQ ID NO:58) and C( $\Delta$ 81-90) (SEQ ID NO:59) were  
unable to activate Elongin A, Elongin ABC complexes  
30 containing these same Elongin C mutants were capable of



stimulating the rate of elongation by RNA Polymerase II, suggesting that the Elongin C region between amino acids 71 and 90 is not critical for activation of Elongin A in Elongin ABC complexes assembled by folding all three subunits together.

It is noteworthy that the activity of mutant Elongin ABC complexes does not, in all cases, correlate with the amount of Elongin B and C present. Elongin ABC complexes containing Elongin C internal deletion mutant C( $\Delta$ 71-80) (SEQ ID NO:58) are considerably more active than those containing C( $\Delta$ 81-90) (SEQ ID NO:59), even though Elongin ABC complexes containing C( $\Delta$ 81-90) (SEQ ID NO:59) contain more Elongin B and C. Thus, the results of these experiments demonstrate that binding of Elongin C to Elongin A is not sufficient for activation of Elongin A, and they indicate the importance of the C-terminus of Elongin C for activation of Elongin A.

Further evidence supporting the importance of the C-terminus of Elongin C in activation of Elongin A came from an analysis of a set of clustered alanine scanning mutants in which Elongin C residues between 89 and 112 (SEQ ID NO:75) were mutated three at a time to alanines. As predicted, all C-terminal alanine scanning mutants were capable of binding to Elongin B to form chromatographically isolable Elongin BC complexes (data not shown). In addition, although Elongin BC complexes containing three of these mutants, C(Ala89-91) (SEQ ID NO:65), C(Ala98-100) (SEQ ID NO:68), and C(Ala107-109) (SEQ ID NO:71), were nearly

as active as wild type BC complexes, the activity of BC complexes containing C(Ala92-94) (SEQ ID NO:66), C(Ala95-97) (SEQ ID NO:67), C(Ala101-103) (SEQ ID NO:69), C(Ala104-106) (SEQ ID NO:70), and C(Ala110-112) (SEQ ID NO:72) was significantly impaired (Fig. 15).

Elongin C mutations fall into several classes based on their effects on Elongin C activities (Fig. 16). First, the only Elongin C mutations that had dramatic effects on Elongin B binding fell within a short Elongin C region between amino acids 19 and 30 (SEQ ID NO:10). This is consistent with the possibility that sequences within this region are directly involved in interactions with Elongin B. Deletion mutations in this region, however, were also found to affect the ability of Elongin C to assemble into isolable Elongin ABC complexes and to activate Elongin A transcriptional activity. Thus, it is also possible that some mutations in this region disrupt the overall tertiary structure of Elongin C.

Second, the only Elongin C mutations that had dramatic effects on formation of isolable Elongin ABC complexes without affecting formation of Elongin BC complexes were mutations in the extreme C-terminus of Elongin C. This result, together with our finding that all Elongin C internal deletion mutants (C( $\Delta$ 31-40) (SEQ ID NO:54); C( $\Delta$ 41-50) (SEQ ID NO:55); C( $\Delta$ 51-60) (SEQ ID NO:56); C( $\Delta$ 61-70) (SEQ ID NO:57); C( $\Delta$ 71-80) (SEQ ID NO:58); C( $\Delta$ 81-90) (SEQ ID NO:59); and C( $\Delta$ 91-100) (SEQ ID NO:60), except C( $\Delta$ 21-30) (SEQ ID NO:53), were capable of forming isolable Elongin ABC complexes,

suggests that the C-terminus of Elongin C plays a crucial role in binding Elongin A.

Third, Elongin C mutations that affect formation of Elongin ABC complexes are only a subset of those mutations that affect the elongation activation activity of Elongin A, indicating that binding of Elongin C by Elongin A is not sufficient for activation of Elongin A. Interestingly, the size of the Elongin C region sensitive to mutations that affect activation of Elongin A was dependent on the assay used to measure activation. In one assay, which measured the ability of Elongin C or Elongin BC complexes to stimulate the rate of elongation by RNA Polymerase II in the presence of Elongin A, Elongin C mutations that fell within the entire C-terminal half of the protein (residues 61-112) (SEQ ID NO:76) drastically reduced Elongin C activity. In contrast, in a second assay, which measured the ability of preassembled Elongin ABC complexes to stimulate the rate of elongation by RNA Polymerase II, Elongin C mutations that fell between residues 71 and 90 had a significantly reduced effect on Elongin A activity, indicating that sequences within this Elongin C region are not essential for activation of Elongin A.

#### Examples

##### Identification of Elongin A Domains

###### Example 1 - Materials

Unlabeled ultrapure ribonucleoside 5'-triphosphates were purchased from Pharmacia Biotech Inc. [ $\alpha$ - $^{32}$ P]CTP (>400 Ci/mmol) was obtained from

Amersham Corp. Phenylmethylsulfonyl fluoride (PMSF),  
heparin, and polyvinyl alcohol type II were from Sigma  
Chemical Co. (St. Louis, Mo). Bovine serum albumin  
(Pentex fraction V) was purchased from ICN  
5 ImmunoBiologicals. Glycerol (Spectranalyzed grade) and  
guanidine hydrochloride (electrophoresis grade) were  
obtained from Fisher Scientific.

**Example 2 - Expression and purification of wild type  
and mutant rat Elongin A**

10 Overexpression of rat Elongin A mutants in *E. coli*  
was accomplished using an M13mpET bacteriophage  
expression system (Garrett et al. 1994; Garrett et al.  
1995). Constructs for expression of 6-histidine-tagged  
N- and C-terminal Elongin A deletion mutants, were  
15 prepared by inserting PCR generated fragments of the  
Elongin A cDNA into the Sal I and Bam HI sites of  
M13mpET. Constructs for expression of Elongin A  
internal deletion and point mutants were prepared by  
oligonucleotide-directed mutagenesis (Kunkel, 1985)  
20 using the Muta-Gene M13 *in vitro* mutagenesis kit (Bio-  
Rad). Elongin A mutants were sequenced by the dideoxy  
chain-termination method using a Sequenase kit (United  
States Biochemicals).

To prepare Elongin A mutants, 500 ml cultures of  
25 *E. coli* strain JM109(DE3) was grown to an OD<sub>600</sub> of 0.6  
in Luria broth containing 2.5 mM MgCl<sub>2</sub> at 37°C with  
gentle shaking. Cells were infected with M13mpET  
vectors carrying mutant Elongin A cDNAs at a  
multiplicity of infection of 20. After an additional 2

hours at 37°C, cells were induced with 0.4 mM isopropyl  $\beta$ -D-thiogalactoside, and cultures were incubated for an additional 2.5 hours. Cells were harvested by centrifugation at 2000 x g for 10 min at 4°C. The cell pellets were resuspended in 25 ml of ice-cold 20 mM Tris-HCl (pH 8.0), 10 mM imidazole (pH 8.0), and 1 mg/ml lysozyme and incubated on ice for 30 min. After 2 cycles of freeze-thaw, the suspension was centrifuged at 100,000 x g for 35 min at 4°C. Inclusion bodies were solubilized by resuspension in 25 ml of ice-cold 50 mM Tris-HCl (pH 8.0) containing 6 M guanidine hydrochloride, and the resulting suspension was clarified by centrifugation at 50,000 x g for 20 min at 4°C. Recombinant Elongin A mutants were purified from the supernatant by  $\text{Ni}^{2+}$ -nitrilotriacetic acid-agarose (Invitrogen) affinity chromatography as described (Garrett et al. 1994; Aso et al. 1995b).

**Example 3 - Reconstitution and purification of Elongin complexes containing Elongin A mutants**

Recombinant Elongin B and C were expressed in *E. coli* using the M13mpET bacteriophage expression system and purified as described previously (Garrett et al. 1994; Garrett et al. 1995). Reconstitution of Elongin complexes was carried out essentially as described (Aso et al. 1995b) by refolding ~50  $\mu\text{g}$  of wild type or mutant Elongin A, ~8  $\mu\text{g}$  of Elongin B, and ~8  $\mu\text{g}$  of Elongin C. Following dialysis, the mixtures were centrifuged at 60,000 x g for 15 min at 4°C. The resulting supernatant were applied to TSK SP-NPR

columns (35 mm x 4.6 mm, Hewlett-Packard) equilibrated in 40 mM Hepes-NaOH (pH 7.9), 0.1 mM EDTA, 1 mM DTT, 10% (v/v) glycerol; and 0.1 M KCl and fractionated using a SMART microchromatography system (Pharmacia) at 8°C. The columns were eluted at 0.6 ml/min with a 9 ml linear gradient from 0.1 to 0.8 M KCl in the same buffer. Aliquots of each column fraction were analyzed by 12% SDS-polyacrylamide gel electrophoresis (PAGE), and the proteins were visualized by silver staining.

10      **Example 4 -      Preparation of RNA Polymerase II and initiation factors**

RNA Polymerase II (Conaway and Conaway, 1990) and TFIID (rat  $\delta$ , TSK DEAE 5-PW fraction) (Conaway et al. 1992) were purified as described from rat liver nuclear extracts. Recombinant yeast TBP (Conaway et al. 1991) and rat TFIIB (rat  $\alpha$ ) (Tsuboi et al. 1992) were expressed in *E. coli* and purified as described. Recombinant TFIIE was prepared as described (Peterson et al. 1991), except that the 56 kDa subunit was expressed in BL21(DE3)-pLysS. Recombinant TFIIF was purified as described (Tan et al. 1994b) from *E. coli* strain JM109(DE3) infected with M13mpET-RAP30 and M13mpET-RAP74.

20      **Example 5 -      Runoff transcription assays**

25      Unless indicated otherwise, preinitiation complexes were assembled as described (Garrett et al. 1995) by preincubation of 50 ng of the EcoRI to NdeI fragment from pDN-AdML (Conaway and Conaway, 1988) and

approximately 10 ng of recombinant TFIIB, 10 ng of recombinant TFIIF, 7 ng of recombinant TFIIE, 40 ng of TFIIH (rat  $\delta$ , fraction VI), 50 ng of recombinant yeast TBP (AcA 44 fraction), and 0.01 units of RNA Polymerase II. Transcription was initiated by addition of 7 mM MgCl<sub>2</sub>, 50  $\mu$ M ATP, 2  $\mu$ M UTP, 10  $\mu$ M CTP, 50  $\mu$ M GTP, and 10  $\mu$ Ci [ $\alpha$ -<sup>32</sup>P]CTP, either in the presence or absence of Elongin preparations. After incubation at 28°C for the times indicated in the legends, runoff transcripts were analysed by electrophoresis through 6% polyacrylamide, 7.0 M urea gels. Transcription was quantitated using a Molecular Dynamics phosphorimager.

**Example 6 - Oligo(dC)-tailed template assay of elongation by RNA Polymerase II**

Pulse-chase assays were carried out essentially as described (Aso et al. 1995b). 0.01 unit of RNA Polymerase III and 100 ng of pCpGR220S/P/X were incubated at 28°C in the presence of 20 mM Hepes-NaOH, pH 7.9, 20 mM Tris-HCl, pH 7.9, 2% (w/v) polyvinyl alcohol, 0.5 mg/ml bovine serum albumin, 60 mM KCl, 50  $\mu$ M ZnSO<sub>4</sub>, 7 mM MgCl<sub>2</sub>, 0.2 mM dithiothreitol, 3% (v/v) glycerol, 3 units of recombinant RNasin (Promega), 50  $\mu$ M ATP, 50  $\mu$ M GTP, 2  $\mu$ M CTP, and 10  $\mu$ Ci of [ $\alpha$ -<sup>32</sup>P]CTP. After 25 min of labeling, the reactions were chased for 7.5 min following addition of 100  $\mu$ M non-radioactive CTP, 2  $\mu$ M UTP, and the indicated amounts of Elongin preparations. Transcripts were analysed by electrophoresis through 6% polyacrylamide, 7.0 M urea gels.

**Example 7 - Isolation of CDNA encoding *C. elegans* Elongin A**

A homology search of the GeneBank database using rat Elongin A protein sequence as the query revealed that nucleotides 19335 through 21154 of *C. elegans* cosmid R03D7 contained a predicted ORF encoding a protein highly homologous to portions of Elongin A. A  $\lambda$  ZAP *C. elegans* cDNA library was constructed and screened with the 5'-<sup>32</sup>P-labeled oligonucleotide 5'-GAG TTG GTC AGT GCT CGC GTG GTC AAG AAC AGG CTT CAG TAG ATC AAA TGG-3' (SEQ ID NO:77), which corresponds to a portion of the predicted ORF. Hybridization was performed at 65°C for 20 hours in 5x standard saline citrate, 5x Denhardt's solution, 100 mM sodium phosphate, 0.1% sodium dodecyl sulfate, 10% dextran sulfate containing denatured salmon testis DNA (100  $\mu$ g/ml). Three overlapping cDNA clones with inserts of up to 1.8 kb were isolated. Clone CE22, which contained the longest insert, was sequenced on both strands by the dideoxy chaintermination method using a Sequenase kit (United States Biochemicals).

**Example 8 - Expression and purification of *C. elegans* Elongin A**

Histidine-tagged *C. elegans* Elongin A was overexpressed in *E. coli* using a pET16b expression vector (Novagen). The pET16b constructs for expression of histidine-tagged wild type and mutant *C. elegans* Elongin A were prepared by insertion of PCR-generated fragments of the *C. elegans* ORF into the Nde I and Bam HI sites of the pET16b vector. A 100 ml culture of *E.*



*coli* strain BL21(DE3) transformed with pET16b carrying the *C. elegans* Elongin A cDNA was grown to an OD<sub>600</sub> of 0.6 in Luria broth containing 50 µg/ml ampicillin at 37°C. Following induction with 1 mM isopropyl β-D-thiogalactoside, the culture was incubated for an additional 2.5 hours at 37°C. Cells were harvested by centrifugation at 2000 x g for 10 min at 4°C. The cell pellet was resuspended in 5 ml of ice-cold 20 mM Tris-HCl (pH 8.0), 10 mM imidazole (pH 8.0), and 1 mg/ml lysozyme and incubated on ice for 30 min. After 2 cycles of freeze-thaw, the suspension was centrifuged at 100,000 x g for 35 min at 4°C. Inclusion bodies were solubilized by resuspension in 5 ml of ice-cold 50 mM Tris-HCl (pH 8.0) containing 6 M guanidine hydrochloride, and the resulting suspension was clarified by centrifugation at 50,000 x g for 20 min at 4°C. Recombinant wild type and mutant *C. elegans* Elongin A were purified from the supernatant by Ni<sup>2+</sup>-nitrilotriacetic acid-agarose (Invitrogen) affinity chromatography as described (Garrett et al. 1994).

#### Identification of Elongin C Domains

##### **Example 9 - Materials**

Unlabeled ultrapure ribonucleoside 5'-triphosphates were purchased from Pharmacia Biotech Inc. Restriction enzymes were obtained from American Allied Biochemicals or Promega. [α-<sup>32</sup>P]CTP (> 650 Ci/mmol) was from Amersham Corp. Proteinase K and isopropyl β-D-thiogalactoside (IPTG) were purchased from Sigma Chemical Co. Bovine serum albumin (Pentex

fraction V, reagent grade) was obtained from ICN Immunobiologicals. Guanidine hydrochloride (Sequanal grade) was obtained from Pierce Chemical Co. Phenylmethylsulfonyl fluoride (PMSF) was from Sigma Chemical Co. and was dissolved in dimethylsulfoxide to 1 M. Polyvinyl alcohol (average molecular weight 30,000-70,000) was from Sigma Chemical Co. and was dissolved in water to 20% (w/v) and centrifuged or filtered through a 0.2  $\mu$  filter prior to use.

10      **Example 10 - DNA template for transcription**

pDN-AdML (19) plasmid DNA was isolated from *E. coli* using the Triton-lysozyme method (20). Plasmid DNA was banded twice in CsCl-ethidium bromide density gradients, precipitated with ethanol, and dissolved in TE buffer (20 mM Tris-HCl, pH 7.6, 1 mM EDTA). A restriction fragment prepared by digestion of pDN-AdML DNA with EcoRI and NdeI was used as the template in transcription reactions. The fragment was purified from a 1.0% low melting temperature agarose gel using GELase (Epicentre Technologies) according to the manufacturer's instructions. After phenol-chloroform extraction and ethanol precipitation, purified DNA fragments were resuspended in TE buffer.

25      **Example 11 - Preparation of RNA Polymerase II and transcription factors**

RNA Polymerase II (21) and TFIIF (rat  $\delta$ , TSK DEAE 5-PW fraction) (22) were purified as described from rat liver nuclear extracts. Recombinant yeast TBP (23) and

rat TFIIB (rat  $\delta$ ) (24) were expressed in *E. coli* and purified as described. Recombinant TFIIE was prepared as described (25), except that the 56-kDa subunit was expressed in BL21(DE3)-pLysS. Recombinant TFIIF was  
5 purified as described (26) from *E. coli* strain JM109 (DE3) infected with M13mpET-RAP30 and M13mpET-RAP74.

#### Example 12 - Runoff transcription assays

All reaction mixtures were 60  $\mu$ l. Preinitiation  
10 complexes were assembled by preincubation of approximately 10 ng template DNA (EcoRI to NdeI fragment from pDN-AdML), ~10 ng of recombinant TFIIB, ~10 ng of recombinant TFIIF, ~7 ng of recombinant TFIIE, ~40 ng of rat TFIH, ~20 ng of TBP, ~0.01 unit  
15 of RNA Polymerase II, and ~8 units of RNasin in 20 mM Hepes-NaOH (pH 7.9), 20 mM Tris-HCl (pH 7.9), 60 mM KCl, 2 mM DTT, 0.5 mg/ml bovine serum albumin, 2% (w/v) polyvinyl alcohol, and 3% (v/v) glycerol for 30 min at 28°C. Elongin, Elongin subassemblies, or Elongin  
20 subunits were then added to reaction mixtures in the amounts and at the times indicated in the figure legends. Transcription was initiated by addition of 7 mM MgCl<sub>2</sub> and 50  $\mu$ M ATP, 50  $\mu$ M GTP, 10  $\mu$ M CTP, 2  $\mu$ M UTP and 10  $\mu$ Ci [ $\alpha$ -<sup>32</sup>P]CTP. After incubation of reaction  
25 mixtures for 9 min at 28°C, runoff transcripts were analyzed by electrophoresis through 6% polyacrylamide gels containing 7.0 M urea. Transcription was quantitated using a Molecular Dynamics phosphorimager.

**Example 13 - Construction of Elongin C mutants**

Elongin C mutants were constructed by oligonucleotide-directed mutagenesis (27) of M13mpET-Elongin C (16) with the Muta-Gene M13 *in vitro* mutagenesis kit (Bio-Rad) and confirmed by dideoxy DNA sequencing with the *fmol* DNA Sequencing System (Promega). Mutagenic oligonucleotides included 15 nucleotides from the parental rat Elongin C sequence (16) on either side of the deletion point. Mutagenic oligonucleotides for alanine scanning mutagenesis included 12 nucleotides from the parental rat Elongin C on either side of the alanine substitution point.

**Example 14 - Expression and purification of Elongin subunits**

Histidine-tagged Elongin A was overexpressed in *E. coli* using a pET16b expression vector (Novagen). The pET16b-Elongin A construct for expression of histidine-tagged Elongin A was prepared by insertion of a PCR-generated fragment containing the entire rat Elongin A open reading frame (18) into the *Nde*I and *Bam*HI sites of the pET-16b vector. A 1L culture of *E. coli* strain BL21(DE3) transformed with pET16b-Elongin A was grown to an OD<sub>600</sub> of 0.6 in Luria broth (LB) (20) containing 100 µg/ml carbenicillin at 37°C. Following induction with 0.5 mM IPTG, the culture was incubated for an additional 3 hours at 37°C. Cells were harvested by centrifugation at 2000 X g for 10 min at 4°C. The cell pellet was resuspended in 50 ml of ice-cold 20 mM Tris-HCl (pH 8.0), 10 mM imidazole (pH 8.0), and 1 mg/ml

lysozyme and incubated on ice for 30 min. After 2 cycles of freeze-thaw, the suspension was centrifuged at 100,000 X g for 35 min. Inclusion bodies were solubilized by resuspension in 50 ml of ice-cold 6 M guanidine hydrochloride, 40 mM Tris-HCl (pH 8.0), 10 mM imidazole (pH 8.0), 0.5 mM PMSF, and 0.5 M KCl, and the resulting suspension was clarified by centrifugation at 100,000 X g for 35 min.

Recombinant Elongin A was purified from the supernatants by  $\text{Ni}^{2+}$ -nitrilotriacetic acid-agarose (Invitrogen) affinity chromatography.  $\text{Ni}^{2+}$  chromatography was performed at 4°C. 10 ml of supernatant was applied to a 2 ml  $\text{Ni}^{2+}$ -column pre-equilibrated with 6 M guanidine hydrochloride, 20 mM Tris-HCl (pH 7.9), 10 mM imidazole (pH 8.0), 0.5 M KCl, and 0.5 mM PMSF. The column was washed with 10 ml of 5.7 M guanidine hydrochloride, 40 mM Tris-HCl (pH 7.9), 40 mM imidazole (pH 8.0), and 0.5 mM PMSF, and recombinant Elongin A was eluted with 4.2 M guanidine hydrochloride, 40 mM Tris-HCl (pH 7.9), 300 mM imidazole (pH 8.0), and 0.5 mM PMSF.

Overexpression of Elongin B and wild type and mutant Elongin C was accomplished using the M13mpET bacteriophage expression system (16,17). A 100 ml culture of *E. coli* strain JM109 (DE3) (Promega) was grown to an  $\text{OD}_{600}$  of 0.6 in Luria broth at 37°C. Cells were infected with M13pET bacteriophage carrying the wild type rat Elongin B or wild type or mutant rat Elongin C cDNAs at a multiplicity of infection of 10-20. After an additional 2 hours at 37°C, cells were

induced with 0.5 mM IPTG, and cultures were incubated an additional 3 hours. Cells were harvested by centrifugation at 2000 X g for 10 min at 4°C. The cell pellet was resuspended in 7 ml of 20 mM Tris-HCl (pH 8.0), 10 mM imidazole (pH 8.0), and 1 mg/ml lysozyme and incubated on ice for 30 min. After 2 cycles of freeze-thaw, the suspension was centrifuged at 100,000 X g for 35 min. Inclusion bodies were solubilized by resuspension in 7 ml of ice-cold 6 M guanidine hydrochloride, 40 mM TrisHCl (pH 8.0), 10 mM imidazole (pH 8.0), 0.5 mM PMSF, and 0.5 M KCl, and the resulting suspension was clarified by centrifugation at 100,000 X g for 35 min. Wild type Elongin B and wild type and mutant Elongin C were purified using Ni<sup>2+</sup>-column chromatography as described above.

**Example 15 - Assay of Elongin BC complex formation**

~6 µg of Elongin B was mixed with ~6 µg of either wild type or mutant Elongin C and diluted 5 fold with 40 mM Hepes-NaOH (pH 7.9), 100 mM KCl, 2 mM DTT, 50 µM ZnSO<sub>4</sub>, 0.1 mM EDTA, and 10% (v/v) glycerol. After incubation for 90 min on ice, the mixtures were dialyzed at 4°C overnight against 40 mM Tris-HCl (pH 7.9), 0.1 mM EDTA, 10% (v/v) glycerol, and 40 mM KCl. Following dialysis, the mixtures were centrifuged at 60,000 X g for 15 min at 4°C. The resulting supernatants were applied to TSK DEAE-NPR columns (35 mm X 4.6 mm, Toso-Haas) pre-equilibrated in 40 mM Tris-HCl (pH 7.9), 0.1 mM EDTA, 1 mM DTT, 10% (v/v) glycerol, and 40 mM KCl and fractionated using a SMART

microchromatography system (Pharmacia) at 8°C. The columns were eluted at 0.3 ml/min with a 3 ml linear gradient from 0.04 to 0.5 M KCl in 40 mM Tris-HCl (pH 7.9), 0.1 mM EDTA, 1 mM DTT, and 10% (v/v) glycerol. Aliquots of each column fraction were analyzed by 10% Tris-Tricine SDS-polyacrylamide gel electrophoresis (28), and the proteins were visualized by silver staining.

#### Example 16 - Assay of Elongin ABC complex formation

~45 µg of Elongin A, ~6 µg of Elongin B, and ~6 µg of either wild type or mutant Elongin C were diluted 5 fold with 40 mM Hepes-NaOH (pH 7.9), 100 mM KCl, 50 µM ZnSO<sub>4</sub>, and 10% (v/v) glycerol. After incubation for 90 min on ice, the mixtures were dialyzed at 4°C overnight against 40 mM Tris-HCl (pH 7.9), 0.1 mM EDTA, 10% (v/v) glycerol, and 40 mM KCl. Following dialysis, the mixtures were centrifuged at 60,000 X g for 15. min at 4°C. The resulting supernatants were applied to TSK SP-NPR columns (35 mm X 4.6 mm, Toso-Haas) pre-equilibrated in 40 mM Hepes-NaOH (pH 7.9), 1 mM DTT, 10% (v/v) glycerol, and 0.1 M KCl and fractionated using a SMART microchromatography system (Pharmacia) at 8°C. The columns were eluted at 0.6 ml/min with a 9 ml linear gradient from 0.1 to 0.8 M KCl in 40 mM Hepes-NaOH (pH 7.9), 1 mM DTT, and 10% (v/v) glycerol. Aliquots of each column fraction were analyzed by 10% Tris-Tricine SDS-polyacrylamide gel electrophoresis (28), and the proteins were visualized by silver staining.

## SEQUENCE LISTING

## (1) GENERAL INFORMATION:

- (i) APPLICANT:
  - (A) NAME: OKLAHOMA MEDICAL RESEARCH FOUNDATION
  - (B) STREET: 800 RESEARCH PARKWAY, SUITE 100
  - (C) CITY: OKLAHOMA CITY
  - (D) STATE: OKLAHOMA
  - (E) COUNTRY: US
  - (F) POSTAL CODE (ZIP): 73104
  - (G) TELEPHONE: (405) 271-7660
  - (H) TELEFAX: (405) 271-3153
  - (I) TELEX: N/A
- (ii) TITLE OF INVENTION: ELONGIN A AND C FUNCTIONAL DOMAINS
- (iii) NUMBER OF SEQUENCES: 77
- (iv) CORRESPONDENCE ADDRESS:
  - (A) ADDRESSEE: SIDLEY & AUSTIN
  - (B) STREET: 1201 ELM STREET, SUITE 4500
  - (C) CITY: DALLAS
  - (D) STATE: TX
  - (E) COUNTRY: US
  - (F) ZIP: 75270-2197
- (v) COMPUTER READABLE FORM:
  - (A) MEDIUM TYPE: Floppy disk
  - (B) COMPUTER: IBM PC compatible
  - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
  - (D) SOFTWARE: PatentIn Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:
  - (A) APPLICATION NUMBER:
  - (B) FILING DATE:
  - (C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:
  - (A) NAME: HANSEN, EUGENIA S.
  - (B) REGISTRATION NUMBER: 31,966
  - (C) REFERENCE/DOCKET NUMBER: 11146/07502
- (ix) TELECOMMUNICATION INFORMATION:
  - (A) TELEPHONE: 214-981-3300
  - (B) TELEFAX: 214-981-3400

## (2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 773 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: not relevant
  - (D) TOPOLOGY: not relevant
- (ii) MOLECULE TYPE: protein



## (ix) FEATURE:

(A) NAME/KEY: Protein

(B) LOCATION: 1..773

(D) OTHER INFORMATION: /note= "entire amino acid sequence of Elongin A"

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## (2) INFORMATION FOR SEQ ID NO:2:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 730 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..730
- (D) OTHER INFORMATION: /note= "amino acids 1-730 of

Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

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 35 40 45

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 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
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 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
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 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
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 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
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 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
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 Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn  
 545 550 555 560  
 Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu  
 565 570 575  
 Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu  
 580 585 590  
 Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val  
 595 600 605  
 His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser  
 610 615 620  
 Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu  
 625 630 635 640  
 Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys  
 645 650 655  
 Gly Arg Gln Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro  
 660 665 670  
 Arg Asp Val Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala  
 675 680 685

Val Pro Glu Lys Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser  
 690 695 700

Ser His Val Pro Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro  
 705 710 715 720

Glu Glu Leu Ala Tyr Glu Gly Pro Ser Thr  
 725 730

## (2) INFORMATION FOR SEQ ID NO:3:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 680 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..680
- (D) OTHER INFORMATION: /note= "amino acids 1-680 of

Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495

```

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala
      500                      505                      510

Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg
      515                      520                      525

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
      530                      535                      540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
      545                      550                      555                      560

Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu
      565                      570                      575

Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu
      580                      585                      590

Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val
      595                      600                      605

His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser
      610                      615                      620

Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu
      625                      630                      635                      640

Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys
      645                      650                      655

Gly Arg Gln Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro
      660                      665                      670

Arg Asp Val Arg Arg Arg Gln Glu
      675                      680

```

## (2) INFORMATION FOR SEQ ID NO:4:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 374 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..374
- (D) OTHER INFORMATION: /note= "amino acids 400-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```

Thr Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys
1           5           10           15

Lys Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly
20           25           30

```



Leu Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala  
           35                                  40                                  45  
 Gln Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro  
           50                                  55                                  60  
 Ala Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu  
           65                                  70                                  75                                  80  
 Pro Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg  
                                   85                                  90                                  95  
 Pro Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys  
                                   100                                  105                                  110  
 Ala Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg  
           115                                  120                                  125  
 Arg Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr  
           130                                  135                                  140  
 Leu Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys  
           145                                  150                                  155                                  160  
 Asn Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val  
                                   165                                  170                                  175  
 Leu Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile  
                                   180                                  185                                  190  
 Glu Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys  
           195                                  200                                  205  
 Val His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu  
           210                                  215                                  220  
 Ser Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg  
           225                                  230                                  235                                  240  
 Leu Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro  
                                   245                                  250                                  255  
 Lys Gly Arg Gln Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro  
           260                                  265                                  270  
 Pro Arg Asp Val Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala  
           275                                  280                                  285  
 Ala Val Pro Glu Lys Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly  
           290                                  295                                  300  
 Ser Ser His Val Pro Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser  
           305                                  310                                  315                                  320  
 Pro Glu Glu Leu Ala Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu  
           325                                  330                                  335  
 Ala Pro Val Ala Ser Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala  
           340                                  345                                  350

Val Lys Lys Ile Ala Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys  
 355 360 365

Asn Arg Phe Ser Arg Arg  
 370

## (2) INFORMATION FOR SEQ ID NO:5:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 331 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..331
- (D) OTHER INFORMATION: /note= "amino acids 400-730 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Thr Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys  
 1 5 10 15

Lys Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly  
 20 25 30

Leu Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala  
 35 40 45

Gln Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro  
 50 55 60

Ala Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu  
 65 70 75 80

Pro Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg  
 85 90 95

Pro Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys  
 100 105 110

Ala Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg  
 115 120 125

Arg Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr  
 130 135 140

Leu Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys  
 145 150 155 160

Asn Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val  
 165 170 175

Leu Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile  
 180 185 190

Glu Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys  
 195 200 205  
 Val His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu  
 210 215 220  
 Ser Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg  
 225 230 235 240  
 Leu Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro  
 245 250 255  
 Lys Gly Arg Gln Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro  
 260 265 270  
 Pro Arg Asp Val Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala  
 275 280 285  
 Ala Val Pro Glu Lys Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly  
 290 295 300  
 Ser Ser His Val Pro Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser  
 305 310 315 320  
 Pro Glu Glu Leu Ala Tyr Glu Gly Pro Ser Thr  
 325 330

## (2) INFORMATION FOR SEQ ID NO:6:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 281 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..281
- (D) OTHER INFORMATION: /note= "amino acids 400-680 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Thr Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys  
 1 5 10 15  
 Lys Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly  
 20 25 30  
 Leu Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala  
 35 40 45  
 Gln Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro  
 50 55 60  
 Ala Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu  
 65 70 75 80

(2) INFORMATION FOR SEO ID NO:7:

SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

(ix) FEATURE:

- (A) NAME/KEY: Peptide  
(B) LOCATION: 1..20  
(D) OTHER INFORMATION: /note= "amino acids 546-565 of

Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn Asn  
1 5 10 15

Ile Asp Ser Ile  
20

## (2) INFORMATION FOR SEQ ID NO:8:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..12
- (D) OTHER INFORMATION: /note= "amino acids 549-560 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn  
1 5 10

## (2) INFORMATION FOR SEQ ID NO:9:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "entire amino acid sequence of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala  
1 5 10 15  
Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys  
20 25 30  
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly  
35 40 45  
Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu  
50 55 60  
Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys  
65 70 75 80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala  
85 90 95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys  
100 105 110

## (2) INFORMATION FOR SEQ ID NO:10:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..12
- (D) OTHER INFORMATION: /note= "amino acids 19-30 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile  
1 5 10

## (2) INFORMATION FOR SEQ ID NO:11:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 13 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..13
- (D) OTHER INFORMATION: /note= "amino acids 100-112 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys  
1 5 10

## (2) INFORMATION FOR SEQ ID NO:12:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

(ix) FEATURE:  
    (A) NAME/KEY: Peptide  
    (B) LOCATION: 1..12  
    (D) OTHER INFORMATION: /note= "amino acids 60-71 of  
Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Val Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser  
1                    5                    10

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:  
    (A) LENGTH: 22 amino acids  
    (B) TYPE: amino acid  
    (C) STRANDEDNESS: not relevant  
    (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:  
    (A) NAME/KEY: Peptide  
    (B) LOCATION: 1..22  
    (D) OTHER INFORMATION: /note= "amino acids 91-112 of  
Elongin C"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala  
1                    5                    10                    15  
  
Ala Asn Phe Leu Asp Cys  
                    20

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:  
    (A) LENGTH: 171 amino acids  
    (B) TYPE: amino acid  
    (C) STRANDEDNESS: not relevant  
    (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:  
    (A) NAME/KEY: Peptide  
    (B) LOCATION: 1..171  
    (D) OTHER INFORMATION: /note= "amino acids 520-690 of  
Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Glu Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val  
1                    5                    10                    15  
  
Tyr Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His  
                    20                    25                    30

Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu  
           35                          40                          45  
 Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys  
           50                          55                          60  
 Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile  
   65                          70                          75                          80  
 Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys  
                           85                          90                          95  
 Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg  
                          100                         105                         110  
 Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile  
                          115                         120                         125  
 Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala  
                          130                         135                         140  
 Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln  
  145                         150                         155                         160  
 Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro  
                          165                         170

## (2) INFORMATION FOR SEQ ID NO:15:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 16 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..16
- (D) OTHER INFORMATION: /note= "amino acids 157-172 of VHL protein"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Thr Leu Lys Glu Arg Cys Leu Gln Val Val Arg Ser Leu Val Lys Pro  
 1                          5                          10                         15

## (2) INFORMATION FOR SEQ ID NO:16:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein



## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..12
- (D) OTHER INFORMATION: /note= "consensus sequence"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Thr Leu Xaa Xaa Xaa Cys Xaa Xaa Val Xaa Xaa Xaa  
 1 5 10

## (2) INFORMATION FOR SEQ ID NO:17:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 630 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..630
- (D) OTHER INFORMATION: /note= "amino acids 1-630 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15  
 Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540  
 Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn  
 545 550 555 560  
 Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu  
 565 570 575  
 Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu  
 580 585 590  
 Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val  
 595 600 605  
 His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser  
 610 615 620  
 Trp Arg Glu Met Tyr Leu  
 625 630

## (2) INFORMATION FOR SEQ ID NO:18:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 535 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..535
- (D) OTHER INFORMATION: /note= "amino acids 1-535 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15  
 Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
                                   85                                  90                                  95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
                                   100                                  105                                  110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
                                   115                                  120                                  125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
                                   130                                  135                                  140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
                                   145                                  150                                  155                                  160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
                                   165                                  170                                  175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
                                   180                                  185                                  190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
                                   195                                  200                                  205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
                                   210                                  215                                  220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
                                   225                                  230                                  235                                  240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
                                   245                                  250                                  255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
                                   260                                  265                                  270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
                                   275                                  280                                  285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
                                   290                                  295                                  300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
                                   305                                  310                                  315                                  320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
                                   325                                  330                                  335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
                                   340                                  345                                  350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
                                   355                                  360                                  365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
                                   370                                  375                                  380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
                                   385                                  390                                  395                                  400

Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415

Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430

Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460

Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480

Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510

Phe Ser Ser Pro Gln Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525

Met Asn Ser Lys Met Gln Val  
 530 535

## (2) INFORMATION FOR SEQ ID NO:19:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 400 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: not relevant  
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide  
 (B) LOCATION: 1..400  
 (D) OTHER INFORMATION: /note= "amino acids 1-400 of

Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400

## (2) INFORMATION FOR SEQ ID NO:20:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 94 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..94

(D) OTHER INFORMATION: /note= "amino acids 680-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

```

Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile
1           5           10           15
Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn
          20           25           30
Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly
          35           40           45
Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val
          50           55           60
Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met
65           70           75           80
Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
          85           90

```

## (2) INFORMATION FOR SEQ ID NO:21:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 733 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..733

(D) OTHER INFORMATION: /note= "amino acids 1-400 and 441-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

```

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
1           5           10           15

```

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335



Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Ser Lys Asn Leu Asn Ser Ala Gln Lys Leu Pro Lys Ala Asn Glu Asn  
 405 410 415  
 Lys Ser Asp Lys Leu Gln Pro Ala Gly Ala Glu Pro Thr Arg Pro Arg  
 420 425 430  
 Lys Val Pro Thr Asp Val Leu Pro Ala Leu Pro Asp Ile Pro Leu Pro  
 435 440 445  
 Ala Ile Gln Thr Asn Tyr Arg Pro Leu Pro Ser Leu Glu Leu Ile Ser  
 450 455 460  
 Ser Phe Gln Pro Lys Arg Lys Ala Phe Ser Ser Pro Gln Glu Glu Glu  
 465 470 475 480  
 Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val Tyr  
 485 490 495  
 Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His Gln  
 500 505 510  
 Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu Val  
 515 520 525  
 Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys Thr  
 530 535 540  
 Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile Glu  
 545 550 555 560  
 Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys Glu  
 565 570 575  
 Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu  
 580 585 590  
 Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg  
 595 600 605  
 Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe  
 610 615 620  
 Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu  
 625 630 635 640  
 Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys  
 645 650 655

Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser  
 660 665 670  
 Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro  
 675 680 685  
 Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser  
 690 695 700  
 Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala  
 705 710 715 720  
 Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg  
 725 730

## (2) INFORMATION FOR SEQ ID NO:22:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 733 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..733
- (D) OTHER INFORMATION: /note= "amino acids 1-440 and 481-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15  
 Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ala Leu Pro Asp Ile Pro Leu Pro  
 435 440 445  
 Ala Ile Gln Thr Asn Tyr Arg Pro Leu Pro Ser Leu Glu Leu Ile Ser  
 450 455 460

```

Ser Phe Gln Pro Lys Arg Lys Ala Phe Ser Ser Pro Gln Glu Glu Glu
465                               470                               475                               480

Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val Tyr
                               485                               490                               495

Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His Gln
                               500                               505                               510

Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu Val
                               515                               520                               525

Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys Thr
530                               535                               540

Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile Glu
545                               550                               555                               560

Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys Glu
                               565                               570                               575

Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu
                               580                               585                               590

Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg
                               595                               600                               605

Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe
610                               615                               620

Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu
625                               630                               635                               640

Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys
                               645                               650                               655

Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser
                               660                               665                               670

Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro
675                               680                               685

Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser
690                               695                               700

Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala
705                               710                               715                               720

Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
                               725                               730

```

## (2) INFORMATION FOR SEQ ID NO:23:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 733 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: not relevant
  - (D) TOPOLOGY: not relevant

- (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

(A) NAME/KEY: Protein  
 (B) LOCATION: 1..733  
 (D) OTHER INFORMATION: /note= "amino acids 1-480 and  
 521-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15  
 Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285

Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val Tyr  
 485 490 495  
 Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His Gln  
 500 505 510  
 Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu Val  
 515 520 525  
 Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys Thr  
 530 535 540  
 Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile Glu  
 545 550 555 560  
 Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys Glu  
 565 570 575  
 Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu  
 580 585 590  
 Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg  
 595 600 605

Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe  
610 615 620

Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu  
625 630 635 640

Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys  
645 650 655

Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser  
660 665 670

Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro  
675 680 685

Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser  
690 695 700

Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala  
705 710 715 720

Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg  
725 730

## (2) INFORMATION FOR SEQ ID NO:24:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 748 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..748
- (D) OTHER INFORMATION: /note= "amino acids 1-520 and 546-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415



Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Lys Met Met Thr Leu His Gln Gln  
 515 520 525  
 Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu Val Gly  
 530 535 540  
 Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys Thr Pro  
 545 550 555 560  
 Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile Glu Glu  
 565 570 575  
 Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys Glu Glu  
 580 585 590  
 Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu Gln  
 595 600 605  
 Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg Ser  
 610 615 620  
 Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe Val  
 625 630 635 640  
 Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu Lys  
 645 650 655  
 Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys Pro  
 660 665 670  
 Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser Ser  
 675 680 685  
 Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro Ser  
 690 695 700  
 Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser Tyr  
 705 710 715 720  
 Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala Lys  
 725 730 735

Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg  
 740 745

## (2) INFORMATION FOR SEQ ID NO:25:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 753 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..753
- (D) OTHER INFORMATION: /note= "amino acids 1-545 and 566-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

```

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
 1             5             10             15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
 20             25             30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
 35             40             45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
 50             55             60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
 65             70             75             80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
 85             90             95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
 100            105            110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
 115            120            125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
 130            135            140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
 145            150            155            160

Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
 165            170            175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
 180            185            190

Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
 195            200            205

```

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525

```

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
530                               535                               540

Pro Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu
545                               550                               555                               560

Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
565                               570                               575

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
580                               585                               590

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
595                               600                               605

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
610                               615                               620

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
625                               630                               635                               640

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
645                               650                               655

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
660                               665                               670

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
675                               680                               685

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
690                               695                               700

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
705                               710                               715                               720

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
725                               730                               735

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
740                               745                               750

```

Arg

## (2) INFORMATION FOR SEQ ID NO:26:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 753 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..753
- (D) OTHER INFORMATION: /note= "amino acids 1-565 and 586-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15  
 Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 490  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540  
 Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn  
 545 550 555 560  
 Asn Ile Asp Ser Ile Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His  
 565 570 575  
 Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg  
 580 585 590  
 Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met  
 595 600 605  
 Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr  
 610 615 620  
 Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala  
 625 630 635 640

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg  
                     645                    650                    655  
 Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys  
                     660                    665                    670  
 Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro  
                     675                    680                    685  
 Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala  
                     690                    695                    700  
 Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser  
                     705                    710                    715                    720  
 Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala  
                     725                    730                    735  
 Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg  
                     740                    745                    750  
 Arg

## (2) INFORMATION FOR SEQ ID NO:27:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 748 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: not relevant
  - (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..748
- (D) OTHER INFORMATION: /note= "amino acids 1-585 and 611-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1                    5                    10                    15  
 Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
                     20                    25                    30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
                     35                    40                    45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
                     50                    55                    60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
                     65                    70                    75                    80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
                     85                    90                    95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415



Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540  
 Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn  
 545 550 555 560  
 Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu  
 565 570 575  
 Glu Pro Val Leu Glu Arg Cys Thr Pro His Arg Asp Phe Lys Glu Glu  
 580 585 590  
 Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg Leu Gln  
 595 600 605  
 Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile Arg Ser  
 610 615 620  
 Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe Val  
 625 630 635 640  
 Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu Lys  
 645 650 655  
 Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys Pro  
 660 665 670  
 Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser Ser  
 675 680 685  
 Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro Ser  
 690 695 700  
 Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser Tyr  
 705 710 715 720  
 Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala Lys  
 725 730 735

Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg  
           740                                  745

## (2) INFORMATION FOR SEQ ID NO:28:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 733 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..733
- (D) OTHER INFORMATION: /note= "amino acids 1-610 and 651-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

```

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
 1                     5                     10                     15
Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
                20                     25                     30
Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
                35                     40                     45
Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
 50                     55                     60
Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
 65                     70                     75                     80
Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
                85                     90                     95
Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
                100                     105                     110
Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
                115                     120                     125
Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
                130                     135                     140
Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
 145                     150                     155                     160
Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
                165                     170                     175
Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
                180                     185                     190
Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
                195                     200                     205

```

Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525

```

Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu
 530                               535                               540

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545                               550                               555                               560

Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu
                               565                               570                               575

Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu
                               580                               585                               590

Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val
                               595                               600                               605

His Cys His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met Ala Phe
                               610                               615                               620

Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg Arg Arg Gln Glu
625                               630                               635                               640

Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys Val Arg Ile Lys
                               645                               650                               655

Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser
                               660                               665                               670

Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro
                               675                               680                               685

Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser
                               690                               695                               700

Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala
705                               710                               715                               720

Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg
                               725                               730

```

## (2) INFORMATION FOR SEQ ID NO:29:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 733 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..733
- (D) OTHER INFORMATION: /note= "amino acids 1-650 and 691-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

```

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
 1             5             10             15

```

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335

Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540  
 Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn  
 545 550 555 560  
 Asn Ile Asp Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu  
 565 570 575  
 Glu Pro Val Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu  
 580 585 590  
 Glu Cys Asn His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val  
 595 600 605  
 His Cys His Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser  
 610 615 620  
 Trp Arg Glu Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu  
 625 630 635 640  
 Arg Leu Leu Thr Asn Asn Ile Arg Ser Ala Glu Lys Val Arg Ile Lys  
 645 650 655

Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro Ala Ser Asn Ser  
660 665 670

Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala Tyr Glu Gly Pro  
675 680 685

Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser Ser Ser Val Ser  
690 695 700

Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala Pro Met Met Ala  
705 710 715 720

Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg Arg  
725 730

## (2) INFORMATION FOR SEQ ID NO:30:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 733 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..733
- (D) OTHER INFORMATION: /note= "amino acids 1-690 and 731-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
115 120 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
130 135 140

Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460



## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

```

Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala Phe Ser Ser
1           5           10           15
Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser
20           25           30
Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met
35           40           45
Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp
50           55           60
Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val
65           70           75           80
Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn
85           90           95
His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His
100          105          110
Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu
115          120          125
Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu
130          135          140
Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln
145          150          155          160
Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val
165          170          175
Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu
180          185          190
Lys Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val
195          200          205
Pro Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu
210          215          220
Ala Tyr Glu Gly Pro Ser Thr
225          230

```

## (2) INFORMATION FOR SEQ ID NO:33:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 201 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..201

(D) OTHER INFORMATION: /note= "amino acids 500-700 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

```

Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala Phe Ser Ser
 1             5             10             15
Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser
 20             25             30
Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met
 35             40             45
Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp
 50             55             60
Ser Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val
 65             70             75             80
Leu Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn
 85             90             95
His Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His
100            105            110
Arg Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu
115            120            125
Met Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu
130            135            140
Thr Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln
145            150            155            160
Ala Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val
165            170            175
Arg Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu
180            185            190
Lys Val Arg Ile Lys Pro Ala Pro Tyr
195            200

```

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..24
- (D) OTHER INFORMATION: /note= "amino acids 545-568 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn  
 1 5 10 15  
 Asn Ile Asp Ser Ile Phe Glu Val  
 20

## (2) INFORMATION FOR SEQ ID NO:35:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 769 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..769
- (D) OTHER INFORMATION: /note= "amino acids 1-544 and 549-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15  
 Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175

Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495

Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540  
 Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser  
 545 550 555 560  
 Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu  
 565 570 575  
 Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His  
 580 585 590  
 Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg  
 595 600 605  
 Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met  
 610 615 620  
 Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr  
 625 630 635 640  
 Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala  
 645 650 655  
 Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg  
 660 665 670  
 Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys  
 675 680 685  
 Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro  
 690 695 700  
 Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala  
 705 710 715 720  
 Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser  
 725 730 735  
 Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala  
 740 745 750  
 Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg  
 755 760 765  
 Arg

## (2) INFORMATION FOR SEQ ID NO:36:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 769 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: not relevant
  - (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(ix) FEATURE:

(A) NAME/KEY: Protein

(B) LOCATION: 1..769

(D) OTHER INFORMATION: /note= "amino acids 1-548 and 553-773 of Elongin A"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
1 5 10 15  
Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
20 25 30  
Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
35 40 45  
Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
50 55 60  
Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
65 70 75 80  
Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
85 90 95  
Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
100 105 110  
Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
115 120 125  
Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
130 135 140  
Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
145 150 155 160  
Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
165 170 175  
Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
180 185 190  
Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
195 200 205  
Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
210 215 220  
His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
225 230 235 240  
His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
245 250 255  
Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
260 265 270

Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540  
 Pro Lys Met Met Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser  
 545 550 555 560  
 Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu  
 565 570 575  
 Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His  
 580 585 590

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg  
 595 600 605  
 Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met  
 610 615 620  
 Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr  
 625 630 635 640  
 Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala  
 645 650 655  
 Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg  
 660 665 670  
 Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys  
 675 680 685  
 Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro  
 690 695 700  
 Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala  
 705 710 715 720  
 Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser  
 725 730 735  
 Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala  
 740 745 750  
 Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg  
 755 760 765  
 Arg

## (2) INFORMATION FOR SEQ ID NO:37:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 769 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..769
- (D) OTHER INFORMATION: /note= "amino acids 1-552 and 557-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15  
 Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30



Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365

Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540  
 Pro Lys Met Met Thr Leu His Gln Val Leu Lys Asn Asn Ile Asp Ser  
 545 550 555 560  
 Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu  
 565 570 575  
 Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His  
 580 585 590  
 Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg  
 595 600 605  
 Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met  
 610 615 620  
 Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr  
 625 630 635 640  
 Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala  
 645 650 655  
 Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg  
 660 665 670  
 Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys  
 675 680 685

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro  
 690 695 700

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala  
 705 710 715 720

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser  
 725 730 735

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala  
 740 745 750

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg  
 755 760 765

Arg

## (2) INFORMATION FOR SEQ ID NO:38:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 769 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..769
- (D) OTHER INFORMATION: /note= "amino acid 1-556 and 561-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15

Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30

Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45

Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60

Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80

Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95

Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110

Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125

Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445

Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540  
 Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Asn Ile Asp Ser  
 545 550 555 560  
 Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu  
 565 570 575  
 Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His  
 580 585 590  
 Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg  
 595 600 605  
 Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met  
 610 615 620  
 Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr  
 625 630 635 640  
 Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala  
 645 650 655  
 Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg  
 660 665 670  
 Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys  
 675 680 685  
 Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro  
 690 695 700  
 Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala  
 705 710 715 720  
 Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser  
 725 730 735  
 Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala  
 740 745 750  
 Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg  
 755 760 765  
 Arg

## (2) INFORMATION FOR SEQ ID NO:39:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 769 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..769
- (D) OTHER INFORMATION: /note= "amino acids 1-560 and 565-773 of Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

```

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg
 1           5           10           15
Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys
          20           25           30
Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val
          35           40           45
Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe
          50           55           60
Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg
          65           70           75           80
Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys
          85           90           95
Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr
          100          105          110
Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His
          115          120          125
Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys
          130          135          140
Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys
          145          150          155          160
Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His
          165          170          175
Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu
          180          185          190
Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys
          195          200          205
Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser
          210          215          220

```

His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320  
 Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540

```

Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn
545                      550                      555                      560

Ile Phe Glu Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu
                    565                      570                      575

Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His
                    580                      585                      590

Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg
                    595                      600                      605

Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met
        610                      615                      620

Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr
625                      630                      635                      640

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
                    645                      650                      655

Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
                    660                      665                      670

Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
        675                      680                      685

Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
        690                      695                      700

Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
705                      710                      715                      720

Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
                    725                      730                      735

Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
                    740                      745                      750

Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
        755                      760                      765

Arg

```

## (2) INFORMATION FOR SEQ ID NO:40:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 769 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..769
- (D) OTHER INFORMATION: /note= "amino acids 1-564 and 569-773 of Elongin A"



(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

Met Ala Ala Glu Ser Ala Leu Gln Val Val Glu Lys Leu Gln Ala Arg  
 1 5 10 15  
 Leu Ala Ala Asn Pro Asp Pro Lys Lys Leu Leu Lys Tyr Leu Lys Lys  
 20 25 30  
 Leu Ser Val Leu Pro Ile Thr Val Asp Ile Leu Val Glu Thr Gly Val  
 35 40 45  
 Gly Lys Thr Val Asn Ser Phe Arg Lys His Glu Gln Val Gly Asn Phe  
 50 55 60  
 Ala Arg Asp Leu Val Ala Gln Trp Lys Lys Leu Val Pro Val Glu Arg  
 65 70 75 80  
 Asn Asn Glu Ala Glu Asp Gln Asp Phe Glu Lys Ser Asn Ser Arg Lys  
 85 90 95  
 Arg Pro Arg Asp Val Pro Gln Gln Glu Glu Glu Ala Glu Gly Asn Tyr  
 100 105 110  
 Gln Glu Ser Trp Gln Ala Ser Gly Ser Gln Pro Tyr Ser Pro Glu His  
 115 120 125  
 Arg Gln Lys Lys His Arg Lys Leu Pro Glu Leu Glu Arg Pro His Lys  
 130 135 140  
 Val Ala His Gly His Glu Arg Arg Asp Glu Arg Lys Arg Cys His Lys  
 145 150 155 160  
 Val Ser Pro Pro Tyr Ser Ser Asp Pro Glu Ser Ser Asp Tyr Gly His  
 165 170 175  
 Val Gln Ser Pro Pro Pro Ser Ser Pro His Gln Met Tyr Thr Asp Leu  
 180 185 190  
 Ser Arg Ser Pro Glu Met Asp Gln Glu Pro Ile Val Ser His Pro Lys  
 195 200 205  
 Pro Gly Lys Val His Ser Asn Thr Phe Gln Asp Arg Leu Gly Val Ser  
 210 215 220  
 His Leu Gly Glu His Gln Gly Lys Gly Ala Val Ser Gln Asn Lys Pro  
 225 230 235 240  
 His Lys Ser Ser His Lys Glu Lys Arg Pro Val Asp Ala Arg Gly Asp  
 245 250 255  
 Glu Lys Ser Ser Val Met Gly Arg Glu Lys Ser His Lys Ala Ser Ser  
 260 265 270  
 Lys Glu Glu Ser Arg Arg Leu Leu Ser Glu Asp Ser Ala Lys Glu Lys  
 275 280 285  
 Leu Pro Ser Ser Val Val Lys Lys Glu Lys Asp Arg Glu Gly Asn Ser  
 290 295 300  
 Leu Lys Lys Lys Leu Ser Pro Ala Leu Asp Val Ala Ser Asp Asn His  
 305 310 315 320

Phe Lys Lys Pro Lys His Lys Asp Ser Glu Lys Ile Lys Ser Asp Lys  
 325 330 335  
 Asn Lys Gln Ser Val Asp Ser Val Asp Ser Gly Arg Gly Thr Gly Asp  
 340 345 350  
 Pro Leu Pro Arg Ala Lys Asp Lys Val Pro Asn Asn Leu Lys Ala Gln  
 355 360 365  
 Glu Gly Lys Val Arg Thr Asn Ser Asp Arg Lys Ser Pro Gly Ser Leu  
 370 375 380  
 Pro Lys Val Glu Glu Met Asp Met Asp Asp Glu Phe Glu Gln Pro Thr  
 385 390 395 400  
 Met Ser Phe Glu Ser Tyr Leu Ser Tyr Asp Gln Pro Arg Lys Lys Lys  
 405 410 415  
 Lys Lys Val Val Lys Thr Ser Gly Thr Ala Leu Gly Glu Lys Gly Leu  
 420 425 430  
 Lys Lys Lys Asp Ser Lys Ser Thr Ser Lys Asn Leu Asn Ser Ala Gln  
 435 440 445  
 Lys Leu Pro Lys Ala Asn Glu Asn Lys Ser Asp Lys Leu Gln Pro Ala  
 450 455 460  
 Gly Ala Glu Pro Thr Arg Pro Arg Lys Val Pro Thr Asp Val Leu Pro  
 465 470 475 480  
 Ala Leu Pro Asp Ile Pro Leu Pro Ala Ile Gln Thr Asn Tyr Arg Pro  
 485 490 495  
 Leu Pro Ser Leu Glu Leu Ile Ser Ser Phe Gln Pro Lys Arg Lys Ala  
 500 505 510  
 Phe Ser Ser Pro Gln Glu Glu Glu Glu Ala Gly Phe Thr Gly Arg Arg  
 515 520 525  
 Met Asn Ser Lys Met Gln Val Tyr Ser Gly Ser Lys Cys Ala Tyr Leu  
 530 535 540  
 Pro Lys Met Met Thr Leu His Gln Gln Cys Ile Arg Val Leu Lys Asn  
 545 550 555 560  
 Asn Ile Asp Ser Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu  
 565 570 575  
 Glu Arg Cys Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His  
 580 585 590  
 Val Leu Ile Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg  
 595 600 605  
 Asp Phe Lys Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met  
 610 615 620  
 Tyr Leu Arg Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr  
 625 630 635 640

121

```

Asn Asn Ile Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala
    645                                650                                655
Lys Met Ala Phe Val Asn Ser Val Ala Lys Pro Pro Arg Asp Val Arg
    660                                665                                670
Arg Arg Gln Glu Lys Phe Gly Thr Gly Gly Ala Ala Val Pro Glu Lys
    675                                680                                685
Val Arg Ile Lys Pro Ala Pro Tyr Thr Thr Gly Ser Ser His Val Pro
    690                                695                                700
Ala Ser Asn Ser Ser Ser Ser Phe His Ser Ser Pro Glu Glu Leu Ala
    705                                710                                715                                720
Tyr Glu Gly Pro Ser Thr Ser Ser Ala His Leu Ala Pro Val Ala Ser
    725                                730                                735
Ser Ser Val Ser Tyr Asp Pro Arg Lys Pro Ala Val Lys Lys Ile Ala
    740                                745                                750
Pro Met Met Ala Lys Thr Ile Lys Ala Phe Lys Asn Arg Phe Ser Arg
    755                                760                                765
Arg

```

## (2) INFORMATION FOR SEQ ID NO:41:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 6 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..6
- (D) OTHER INFORMATION: /note= "amino acids 556-561 of

Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

```

Arg Val Leu Lys Asn Asn
1      5

```

## (2) INFORMATION FOR SEQ ID NO:42:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 434 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

(A) NAME/KEY: Protein

(B) LOCATION: 1..434

(D) OTHER INFORMATION: /note= "entire amino acid sequence of *C. elegans*"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

```

Met Pro Glu Thr Asp Glu Glu Lys Val Arg Arg Tyr Thr Glu Cys Leu
 1           5           10           15
Met Asn Gly Ile Asp Pro Lys Arg Ala Leu Lys Arg Leu Tyr Asp Leu
 20           25           30
Asn Val Ser Pro Glu Val Phe Lys Ser Ala Asp Thr Val Gln Cys Val
 35           40           45
Lys Arg Tyr Glu Ser Ser Pro Glu Leu Ala Lys Tyr Ala Lys Arg Val
 50           55           60
Arg Asp Lys Leu Leu Gly Gly Arg Lys Arg Glu Lys Gly Gly Gly Glu
 65           70           75           80
Asp Asp Ala Asp Ile Glu His Thr Ala Leu Lys Lys Ala Lys Lys Glu
 85           90           95
Glu Val Asn Leu Asp Glu Glu Phe Ala Glu Ala Met Lys Ser Gly Val
100           105           110
Ser Ala Gln Ala Ser Ser Ala Pro Arg Ala Thr Val Asp Tyr Ser Lys
115           120           125
Tyr Lys Val Val Lys Arg Val Glu Val Lys Val Glu Pro Lys Pro Glu
130           135           140
Pro Val Asp Val His Glu Gln Gln Ala Ser Ser Ser Ser Met Ser Tyr
145           150           155           160
Gln Arg Glu His Gln Lys Asp Tyr Ala Pro Val Val Pro Thr Cys Lys
165           170           175
Pro Ser Gly Gln Pro Lys Lys Ala Ile Pro Gln Ser Lys Ser Leu His
180           185           190
Ala Asp Glu Asn Met Phe Lys Pro Arg Lys Glu Arg Gln Lys Val Phe
195           200           205
Ala Gly Arg Arg Lys Arg Val Gly Glu Gly Val Ser Thr Leu Val Ser
210           215           220
Leu Cys Gln Thr Val Leu Met Ser His Ile Asp Met Ile Asp His Val
225           230           235           240
Gly Ile Val Pro Phe Asp Leu Leu Lys Pro Val Leu Asp His Ala Ser
245           250           255
Thr Asp Gln Leu Arg His Ile Leu Asp Val Asn Pro Met Leu Val Glu
260           265           270
Asp Ala Asp Glu Met Phe His Glu Met Val Ser Arg Glu Phe Pro Lys
275           280           285

```

Tyr Ala Asn Arg Glu Lys Ser Gly Trp Thr Trp Arg Glu Met Tyr Asp  
 290 295 300  
 Arg Leu Val Glu Lys Lys Gln Lys Lys Glu Asn Asp Lys Leu Glu Met  
 305 310 315 320  
 Leu Thr Ser Arg Ile Gly Lys Ser Asn Ser Ala Gln Ser Gln Gly Arg  
 325 330 335  
 Gln Thr Met Val Ile Asp Met Ala His Thr Arg Val Arg Ser Lys Ser  
 340 345 350  
 Phe Phe Asn Thr Val Lys Asp Ser Gln Val Lys Met Ser Ala Thr Pro  
 355 360 365  
 Ser Ala Leu Gln Leu Ser Gln Ala Arg Lys Asn Val Lys Ile Glu Gly  
 370 375 380  
 Lys Ala Gln Leu Arg Thr Ile Thr Pro Arg Gly Gly Gly Val Pro Ser  
 385 390 395 400  
 Thr Ser Arg Ser Arg Ser Asn Asn Asn Asn Asn Met Asn Asn Gly Leu  
 405 410 415  
 Val Val Lys Lys Thr Ala Pro Leu Met Ala Lys Cys Lys Lys Met Leu  
 420 425 430  
 Lys Arg

## (2) INFORMATION FOR SEQ ID NO:43:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 143 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..143
- (D) OTHER INFORMATION: /note= "amino acids 520-662 of

Elongin A"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

Glu Glu Ala Gly Phe Thr Gly Arg Arg Met Asn Ser Lys Met Gln Val  
 1 5 10 15  
 Tyr Ser Gly Ser Lys Cys Ala Tyr Leu Pro Lys Met Met Thr Leu His  
 20 25 30  
 Gln Gln Cys Ile Arg Val Leu Lys Asn Asn Ile Asp Ser Ile Phe Glu  
 35 40 45  
 Val Gly Gly Val Pro Tyr Ser Val Leu Glu Pro Val Leu Glu Arg Cys  
 50 55 60

124

```

Thr Pro Asp Gln Leu Tyr Arg Ile Glu Glu Cys Asn His Val Leu Ile
65              70              75              80
Glu Glu Thr Asp Gln Leu Trp Lys Val His Cys His Arg Asp Phe Lys
85              90              95
Glu Glu Arg Pro Glu Glu Tyr Glu Ser Trp Arg Glu Met Tyr Leu Arg
100            105            110
Leu Gln Asp Ala Arg Glu Gln Arg Leu Arg Leu Leu Thr Asn Asn Ile
115            120            125
Arg Ser Ala His Ala Asn Lys Pro Lys Gly Arg Gln Ala Lys Met
130            135            140

```

## (2) INFORMATION FOR SEQ ID NO:44:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 341 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..341
- (D) OTHER INFORMATION: /note= "amino acids 94-434 of C.

elegans"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

```

Lys Lys Glu Glu Val Asn Leu Asp Glu Glu Phe Ala Glu Ala Met Lys
1              5              10              15
Ser Gly Val Ser Ala Gln Ala Ser Ser Ala Pro Arg Ala Thr Val Asp
20            25            30
Tyr Ser Lys Tyr Lys Val Val Lys Arg Val Glu Val Lys Val Glu Pro
35            40            45
Lys Pro Glu Pro Val Asp Val His Glu Gln Gln Ala Ser Ser Ser Ser
50            55            60
Met Ser Tyr Gln Arg Glu His Gln Lys Asp Tyr Ala Pro Val Val Pro
65            70            75            80
Thr Cys Lys Pro Ser Gly Gln Pro Lys Lys Ala Ile Pro Gln Ser Lys
85            90            95
Ser Leu His Ala Asp Glu Asn Met Phe Lys Pro Arg Lys Glu Arg Gln
100           105           110
Lys Val Phe Ala Gly Arg Arg Lys Arg Val Gly Glu Gly Val Ser Thr
115           120           125
Leu Val Ser Leu Cys Gln Thr Val Leu Met Ser His Ile Asp Met Ile
130           135           140

```

Asp His Val Gly Ile Val Pro Phe Asp Leu Leu Lys Pro Val Leu Asp  
 145 150 155 160  
 His Ala Ser Thr Asp Gln Leu Arg His Ile Leu Asp Val Asn Pro Met  
 165 170 175  
 Leu Val Glu Asp Ala Asp Glu Met Phe His Glu Met Val Ser Arg Glu  
 180 185 190  
 Phe Pro Lys Tyr Ala Asn Arg Glu Lys Ser Gly Trp Thr Trp Arg Glu  
 195 200 205  
 Met Tyr Asp Arg Leu Val Glu Lys Lys Gln Lys Lys Glu Asn Asp Lys  
 210 215 220  
 Leu Glu Met Leu Thr Ser Arg Ile Gly Lys Ser Asn Ser Ala Gln Ser  
 225 230 235 240  
 Gln Gly Arg Gln Thr Met Val Ile Asp Met Ala His Thr Arg Val Arg  
 245 250 255  
 Ser Lys Ser Phe Phe Asn Thr Val Lys Asp Ser Gln Val Lys Met Ser  
 260 265 270  
 Ala Thr Pro Ser Ala Leu Gln Leu Ser Gln Ala Arg Lys Asn Val Lys  
 275 280 285  
 Ile Glu Gly Lys Ala Gln Leu Arg Thr Ile Thr Pro Arg Gly Gly Gly  
 290 295 300  
 Val Pro Ser Thr Ser Arg Ser Arg Ser Asn Asn Asn Asn Asn Met Asn  
 305 310 315 320  
 Asn Gly Leu Val Val Lys Lys Thr Ala Pro Leu Met Ala Lys Cys Lys  
 325 330 335  
 Lys Met Leu Lys Arg  
 340

## (2) INFORMATION FOR SEQ ID NO:45:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 233 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..233
- (D) OTHER INFORMATION: /note= "amino acids 202-434 of C.

elegans"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

Lys Glu Arg Gln Lys Val Phe Ala Gly Arg Arg Lys Arg Val Gly Glu  
 1 5 10 15

126

Gly Val Ser Thr Leu Val Ser Leu Cys Gln Thr Val Leu Met Ser His  
                   20                  25                  30  
 Ile Asp Met Ile Asp His Val Gly Ile Val Pro Phe Asp Leu Leu Lys  
                   35                  40                  45  
 Pro Val Leu Asp His Ala Ser Thr Asp Gln Leu Arg His Ile Leu Asp  
                   50                  55                  60  
 Val Asn Pro Met Leu Val Glu Asp Ala Asp Glu Met Phe His Glu Met  
                   65                  70                  75                  80  
 Val Ser Arg Glu Phe Pro Lys Tyr Ala Asn Arg Glu Lys Ser Gly Trp  
                   85                  90                  95  
 Thr Trp Arg Glu Met Tyr Asp Arg Leu Val Glu Lys Lys Gln Lys Lys  
                   100                  105                  110  
 Glu Asn Asp Lys Leu Glu Met Leu Thr Ser Arg Ile Gly Lys Ser Asn  
                   115                  120                  125  
 Ser Ala Gln Ser Gln Gly Arg Gln Thr Met Val Ile Asp Met Ala His  
                   130                  135                  140  
 Thr Arg Val Arg Ser Lys Ser Phe Phe Asn Thr Val Lys Asp Ser Gln  
                   145                  150                  155                  160  
 Val Lys Met Ser Ala Thr Pro Ser Ala Leu Gln Leu Ser Gln Ala Arg  
                   165                  170                  175  
 Lys Asn Val Lys Ile Glu Gly Lys Ala Gln Leu Arg Thr Ile Thr Pro  
                   180                  185                  190  
 Arg Gly Gly Gly Val Pro Ser Thr Ser Arg Ser Arg Ser Asn Asn Asn  
                   195                  200                  205  
 Asn Asn Met Asn Asn Gly Leu Val Val Lys Lys Thr Ala Pro Leu Met  
                   210                  215                  220  
 Ala Lys Cys Lys Lys Met Leu Lys Arg  
                   225                  230

## (2) INFORMATION FOR SEQ ID NO:46:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 98 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..98
- (D) OTHER INFORMATION: /note= "amino acids 15-112 of Elongin C"



## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

Asp Ala Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile  
 1 5 10 15  
 Val Lys Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu  
 20 25 30  
 Ser Gly Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe  
 35 40 45  
 Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr  
 50 55 60  
 Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro  
 65 70 75 80  
 Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu  
 85 90 95  
 Asp Cys

## (2) INFORMATION FOR SEQ ID NO:47:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 94 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..94
- (D) OTHER INFORMATION: /note= "amino acids 19-112 of

Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys Arg Glu  
 1 5 10 15  
 His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly Pro Gly  
 20 25 30  
 Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu Ile Pro  
 35 40 45  
 Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys Val Arg  
 50 55 60  
 Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala Pro Glu  
 65 70 75 80  
 Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys  
 85 90

## (2) INFORMATION FOR SEQ ID NO:48:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 90 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..90
- (D) OTHER INFORMATION: /note= "amino acids 23-112 of

Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

Ser	Ser	Asp	Gly	His	Glu	Phe	Ile	Val	Lys	Arg	Glu	His	Ala	Leu	Thr
1				5					10					15	
Ser	Gly	Thr	Ile	Lys	Ala	Met	Leu	Ser	Gly	Pro	Gly	Gln	Phe	Ala	Glu
			20					25					30		
Asn	Glu	Thr	Asn	Glu	Val	Asn	Phe	Arg	Glu	Ile	Pro	Ser	His	Val	Leu
		35					40					45			
Ser	Lys	Val	Cys	Met	Tyr	Phe	Thr	Tyr	Lys	Val	Arg	Tyr	Thr	Asn	Ser
	50					55					60				
Ser	Thr	Glu	Ile	Pro	Glu	Phe	Pro	Ile	Ala	Pro	Glu	Ile	Ala	Leu	Glu
65					70					75				80	
Leu	Leu	Met	Ala	Ala	Asn	Phe	Leu	Asp	Cys						
					85				90						

## (2) INFORMATION FOR SEQ ID NO:49:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 84 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..84
- (D) OTHER INFORMATION: /note= "amino acids 29-112 of

Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

Phe	Ile	Val	Lys	Arg	Glu	His	Ala	Leu	Thr	Ser	Gly	Thr	Ile	Lys	Ala
1				5					10					15	
Met	Leu	Ser	Gly	Pro	Gly	Gln	Phe	Ala	Glu	Asn	Glu	Thr	Asn	Glu	Val
			20					25					30		

[illegible]

(2) INFORMATION FOR SEQ ID NO:50:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 56 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: not relevant
  - (D) TOPOLOGY: not relevant

- (ii) MOLECULE TYPE: peptide

- (ix) FEATURE:

- ```
(A) NAME/KEY: Peptide
(B) LOCATION: 1..56
```

- (D) OTHER INFORMATION: /note= "amino acids 57-112 of Elongin C"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Asn | Glu | Val | Asn | Phe | Arg | Glu | Ile | Pro | Ser | His | Val | Leu | Ser | Lys |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Val | Cys | Met | Tyr | Phe | Thr | Tyr | Lys | Val | Arg | Tyr | Thr | Asn | Ser | Ser | Thr |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Glu | Ile | Pro | Glu | Phe | Pro | Ile | Ala | Pro | Glu | Ile | Ala | Leu | Glu | Leu | Leu |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Met | Ala | Ala | Asn | Phe | Leu | Asp | Cys |     |     |     |     |     |     |     |     |
|     | 50  |     |     |     |     | 55  |     |     |     |     |     |     |     |     |     |

## (2) INFORMATION FOR SEQ ID NO:51:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 97 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: not relevant
  - (D) TOPOLOGY: not relevant

- (ii) MOLECULE TYPE: peptide

- (ix) FEATURE:

- ```
(A) NAME/KEY: Peptide
(B) LOCATION: 1..97
```

- (D) OTHER INFORMATION: /note= "amino acids 1-97 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala  
 1 5 10 15  
 Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys  
 20 25 30  
 Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly  
 35 40 45  
 Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu  
 50 55 60  
 Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys  
 65 70 75 80  
 Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala  
 85 90 95  
 Pro

## (2) INFORMATION FOR SEQ ID NO:52:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 83 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..83
- (D) OTHER INFORMATION: /note= "amino acids 1-83 of Elongin

C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala  
 1 5 10 15  
 Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys  
 20 25 30  
 Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly  
 35 40 45  
 Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu  
 50 55 60  
 Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys  
 65 70 75 80  
 Val Arg Tyr

## (2) INFORMATION FOR SEQ ID NO:53:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 102 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..102
- (D) OTHER INFORMATION: /note= "amino acids 1-20 and 31-112 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
 1           5           10           15
Met Tyr Val Lys Val Lys Arg Glu His Ala Leu Thr Ser Gly Thr Ile
          20           25           30
Lys Ala Met Leu Ser Gly Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn
          35           40           45
Glu Val Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys
          50           55           60
Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
          65           70           75           80
Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
          85           90           95
Ala Asn Phe Leu Asp Cys
          100

```

## (2) INFORMATION FOR SEQ ID NO:54:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 102 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..102
- (D) OTHER INFORMATION: /note= "amino acids 1-30 and 41-112 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
 1           5           10           15

```

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```

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Thr Ile
          20                      25                      30
Lys Ala Met Leu Ser Gly Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn
          35                      40                      45
Glu Val Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys
          50                      55                      60
Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
          65                      70                      75                      80
Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
          85                      90                      95
Ala Asn Phe Leu Asp Cys
          100

```

## (2) INFORMATION FOR SEQ ID NO:55:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 102 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..102

(D) OTHER INFORMATION: /note= "amino acids 1-40 and 51-112 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1          5          10          15
Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
          20          25          30
Arg Glu His Ala Leu Thr Ser Gly Gln Phe Ala Glu Asn Glu Thr Asn
          35          40          45
Glu Val Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys
          50          55          60
Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
          65          70          75          80
Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
          85          90          95
Ala Asn Phe Leu Asp Cys
          100

```

## (2) INFORMATION FOR SEQ ID NO:56:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 102 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..102

(D) OTHER INFORMATION: /note= "amino acids 1-50 and 61-112 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
 1             5             10             15
Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
          20             25             30
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
          35             40             45
Pro Gly Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys
          50             55             60
Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile
65             70             75             80
Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala
          85             90             95
Ala Asn Phe Leu Asp Cys
          100

```

## (2) INFORMATION FOR SEQ ID NO:57:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 102 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..102

(D) OTHER INFORMATION: /note= "amino acids 1-60 and 71-112 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
 1             5             10             15

```

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Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys  
 20 25 30  
 Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly  
 35 40 45  
 Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Ser Lys Val Cys  
 50 55 60  
 Met Tyr Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile  
 65 70 75 80  
 Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala  
 85 90 95  
 Ala Asn Phe Leu Asp Cys  
 100

## (2) INFORMATION FOR SEQ ID NO:58:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 102 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..102
- (D) OTHER INFORMATION: /note= "amino acids 1-70 and 81-112 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala  
 1 5 10 15  
 Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys  
 20 25 30  
 Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly  
 35 40 45  
 Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu  
 50 55 60  
 Ile Pro Ser His Val Leu Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile  
 65 70 75 80  
 Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala  
 85 90 95  
 Ala Asn Phe Leu Asp Cys  
 100



## (2) INFORMATION FOR SEQ ID NO:59:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 102 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..102
- (D) OTHER INFORMATION: /note= "amino acids 1-80 and 91-112 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala  
1 5 10 15  
Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys  
20 25 30  
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly  
35 40 45  
Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu  
50 55 60  
Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys  
65 70 75 80  
Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala  
85 90 95  
Ala Asn Phe Leu Asp Cys  
100

## (2) INFORMATION FOR SEQ ID NO:60:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 102 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..102
- (D) OTHER INFORMATION: /note= "amino acids 1-90 and 101-112 of Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala  
1 5 10 15

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```

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
      20                      25                      30
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
      35                      40                      45
Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
      50                      55                      60
Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
      65                      70                      75                      80
Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Leu Glu Leu Leu Met Ala
      85                      90                      95
Ala Asn Phe Leu Asp Cys
      100

```

## (2) INFORMATION FOR SEQ ID NO:61:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 19-21 of Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1      5      10      15
Met Tyr Ala Ala Ala Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
      20      25      30
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
      35      40      45
Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
      50      55      60
Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
      65      70      75      80
Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
      85      90      95
Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
      100      105      110

```

## (2) INFORMATION FOR SEQ ID NO:62:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 22-24 of Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

Met	Asp	Gly	Glu	Glu	Lys	Thr	Tyr	Gly	Gly	Cys	Glu	Gly	Pro	Asp	Ala
1				5				10						15	
Met	Tyr	Val	Lys	Leu	Ala	Ala	Ala	Asp	Gly	His	Glu	Phe	Ile	Val	Lys
			20					25					30		
Arg	Glu	His	Ala	Leu	Thr	Ser	Gly	Thr	Ile	Lys	Ala	Met	Leu	Ser	Gly
			35				40					45			
Pro	Gly	Gln	Phe	Ala	Glu	Asn	Glu	Thr	Asn	Glu	Val	Asn	Phe	Arg	Glu
			50			55					60				
Ile	Pro	Ser	His	Val	Leu	Ser	Lys	Val	Cys	Met	Tyr	Phe	Thr	Tyr	Lys
65				70					75					80	
Val	Arg	Tyr	Thr	Asn	Ser	Ser	Thr	Glu	Ile	Pro	Glu	Phe	Pro	Ile	Ala
			85					90						95	
Pro	Glu	Ile	Ala	Leu	Glu	Leu	Leu	Met	Ala	Ala	Asn	Phe	Leu	Asp	Cys
			100					105						110	

## (2) INFORMATION FOR SEQ ID NO:63:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 25-27 of Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

Met	Asp	Gly	Glu	Glu	Lys	Thr	Tyr	Gly	Gly	Cys	Glu	Gly	Pro	Asp	Ala
1				5				10						15	

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```

Met Tyr Val Lys Leu Ile Ser Ser Ala Ala Ala Glu Phe Ile Val Lys
      20              25              30
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
      35              40              45
Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
      50              55              60
Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
      65              70              75              80
Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
      85              90              95
Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
      100             105             110

```

## (2) INFORMATION FOR SEQ ID NO:64:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 28-30 of Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1              5              10              15
Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Ala Ala Ala Val Lys
      20              25              30
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
      35              40              45
Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
      50              55              60
Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
      65              70              75              80
Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
      85              90              95
Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys
      100             105             110

```

## (2) INFORMATION FOR SEQ ID NO:65:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 89-91 of Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

Met	Asp	Gly	Glu	Glu	Lys	Thr	Tyr	Gly	Gly	Cys	Glu	Gly	Pro	Asp	Ala
1				5					10					15	
Met	Tyr	Val	Lys	Leu	Ile	Ser	Ser	Asp	Gly	His	Glu	Phe	Ile	Val	Lys
		20					25					30			
Arg	Glu	His	Ala	Leu	Thr	Ser	Gly	Thr	Ile	Lys	Ala	Met	Leu	Ser	Gly
		35				40					45				
Pro	Gly	Gln	Phe	Ala	Glu	Asn	Glu	Thr	Asn	Glu	Val	Asn	Phe	Arg	Glu
	50					55				60					
Ile	Pro	Ser	His	Val	Leu	Ser	Lys	Val	Cys	Met	Tyr	Phe	Thr	Tyr	Lys
65					70				75					80	
Val	Arg	Tyr	Thr	Asn	Ser	Ser	Thr	Ala	Ala	Ala	Glu	Phe	Pro	Ile	Ala
			85					90						95	
Pro	Glu	Ile	Ala	Leu	Glu	Leu	Leu	Met	Ala	Ala	Asn	Phe	Leu	Asp	Cys
		100					105						110		

## (2) INFORMATION FOR SEQ ID NO:66:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 92-94 Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

Met	Asp	Gly	Glu	Glu	Lys	Thr	Tyr	Gly	Gly	Cys	Glu	Gly	Pro	Asp	Ala
1				5					10					15	

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Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys  
 20 25 30  
 Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly  
 35 40 45  
 Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu  
 50 55 60  
 Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys  
 65 70 75 80  
 Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Ala Ala Ala Ile Ala  
 85 90 95  
 Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys  
 100 105 110

## (2) INFORMATION FOR SEQ ID NO:67:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 95-97 of Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala  
 1 5 10 15  
 Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys  
 20 25 30  
 Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly  
 35 40 45  
 Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu  
 50 55 60  
 Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys  
 65 70 75 80  
 Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ala Ala  
 85 90 95  
 Ala Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Leu Asp Cys  
 100 105 110

## (2) INFORMATION FOR SEQ ID NO:68:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 98-100 of

Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

Met	Asp	Gly	Glu	Glu	Lys	Thr	Tyr	Gly	Gly	Cys	Glu	Gly	Pro	Asp	Ala
1				5				10					15		
Met	Tyr	Val	Lys	Leu	Ile	Ser	Ser	Asp	Gly	His	Glu	Phe	Ile	Val	Lys
			20					25					30		
Arg	Glu	His	Ala	Leu	Thr	Ser	Gly	Thr	Ile	Lys	Ala	Met	Leu	Ser	Gly
			35				40					45			
Pro	Gly	Gln	Phe	Ala	Glu	Asn	Glu	Thr	Asn	Glu	Val	Asn	Phe	Arg	Glu
			50			55				60					
Ile	Pro	Ser	His	Val	Leu	Ser	Lys	Val	Cys	Met	Tyr	Phe	Thr	Tyr	Lys
65					70				75					80	
Val	Arg	Tyr	Thr	Asn	Ser	Ser	Thr	Glu	Ile	Pro	Glu	Phe	Pro	Ile	Ala
				85				90						95	
Pro	Ala	Ala	Ala	Leu	Glu	Leu	Leu	Met	Ala	Ala	Asn	Phe	Leu	Asp	Cys
				100				105					110		

## (2) INFORMATION FOR SEQ ID NO:69:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 101-103 of

Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

Met	Asp	Gly	Glu	Glu	Lys	Thr	Tyr	Gly	Gly	Cys	Glu	Gly	Pro	Asp	Ala
1				5				10					15		

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```

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
      20              25              30
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
      35              40              45
Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
      50              55              60
Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
      65              70              75              80
Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
      85              90              95
Pro Glu Ile Ala Ala Ala Ala Leu Met Ala Ala Asn Phe Leu Asp Cys
      100             105             110

```

## (2) INFORMATION FOR SEQ ID NO:70:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 104-106 of Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
1          5          10          15
Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
      20              25              30
Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
      35              40              45
Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
      50              55              60
Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
      65              70              75              80
Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
      85              90              95
Pro Glu Ile Ala Leu Glu Leu Ala Ala Ala Ala Asn Phe Leu Asp Cys
      100             105             110

```



## (2) INFORMATION FOR SEQ ID NO:71:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 107-109 of Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
 1             5             10             15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
      20             25             30

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly
      35             40             45

Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu
 50             55             60

Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys
65             70             75             80

Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala
      85             90             95

Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Ala Ala Leu Asp Cys
100             105             110

```

## (2) INFORMATION FOR SEQ ID NO:72:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Protein
- (B) LOCATION: 1..112
- (D) OTHER INFORMATION: /note= "amino acids 110-112 of Elongin C mutated to alanine"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

```

Met Asp Gly Glu Glu Lys Thr Tyr Gly Gly Cys Glu Gly Pro Asp Ala
 1             5             10             15

Met Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile Val Lys
 20             25             30

```

Arg Glu His Ala Leu Thr Ser Gly Thr Ile Lys Ala Met Leu Ser Gly  
35 40 45  
Pro Gly Gln Phe Ala Glu Asn Glu Thr Asn Glu Val Asn Phe Arg Glu  
50 55 60  
Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr Phe Thr Tyr Lys  
65 70 75 80  
Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu Phe Pro Ile Ala  
85 90 95  
Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn Phe Ala Ala Ala  
100 105 110

## (2) INFORMATION FOR SEQ ID NO:73:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..5
- (D) OTHER INFORMATION: /note= "amino acids 18-22 of

Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

Tyr Val Lys Leu Ile  
1 5

## (2) INFORMATION FOR SEQ ID NO:74:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 13 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..13
- (D) OTHER INFORMATION: /note= "amino acids 18-30 of

Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

Tyr Val Lys Leu Ile Ser Ser Asp Gly His Glu Phe Ile  
1 5 10

## (2) INFORMATION FOR SEQ ID NO:75:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..24

(D) OTHER INFORMATION: /note= "amino acids 89-112 of  
Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

Glu Ile Pro Glu Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu  
1 5 10 15

Met Ala Ala Asn Phe Leu Asp Cys  
20

## (2) INFORMATION FOR SEQ ID NO:76:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 52 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: peptide

## (ix) FEATURE:

- (A) NAME/KEY: Peptide
- (B) LOCATION: 1..52

(D) OTHER INFORMATION: /note= "amino acids 61-112 of  
Elongin C"

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

Asn Phe Arg Glu Ile Pro Ser His Val Leu Ser Lys Val Cys Met Tyr  
1 5 10 15

Phe Thr Tyr Lys Val Arg Tyr Thr Asn Ser Ser Thr Glu Ile Pro Glu  
20 25 30

Phe Pro Ile Ala Pro Glu Ile Ala Leu Glu Leu Leu Met Ala Ala Asn  
35 40 45

Phe Leu Asp Cys  
50

(2) INFORMATION FOR SEQ ID NO:77:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 51 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

GAGTTGGTCA GTGCTCGCGT GGTCAAGAAC AGGCTTCAGT AGATCAAATG G

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## CLAIMS:

1. A substantially purified Elongin A fragment having transcriptional activation activity and capable of binding Elongin BC.
2. The substantially purified Elongin A fragment of claim 1 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:16.
3. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:2.
4. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:3.
5. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:4.
6. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:5.
7. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:6.

8. The substantially purified Elongin A fragment of claim 2 wherein said Elongin A fragment comprises an amino acid sequence as depicted in SEQ ID NO:17.

9. A nucleic acid comprising a nucleotide sequence encoding an Elongin A fragment having transcriptional activation activity and capable of binding to Elongin BC.

10. The nucleic acid of claim 9 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:16.

11. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:2.

12. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:3.

13. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:4.

14. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:5.

15. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:6.

16. The nucleic acid of claim 10 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:17.

17. A substantially purified Elongin A having transcriptional activation activity and capable of binding to Elongin BC.

18. The substantially purified Elongin A of claim 17 comprising an amino acid sequence as depicted in SEQ ID NO:16.

19. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:2.

20. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:3.

21. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:4.

22. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:5.

23. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:6.

24. The substantially purified Elongin A of claim 18 comprising an amino acid sequence as depicted in SEQ ID NO:17.

25. A nucleic acid comprising a nucleotide sequence encoding an Elongin A having transcriptional activation activity and capable of binding to Elongin BC.

26. The nucleic acid of claim 25 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:16.

27. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:2.

28. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:3.



29. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:4.

30. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:5.

31. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:6.

32. The nucleic acid of claim 26 wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:17.

33. A substantially purified Elongin A comprising an amino acid sequence as depicted in SEQ ID NO:42.

34. A nucleic acid encoding an Elongin A comprising a nucleotide sequence encoding an amino acid sequence as depicted in SEQ ID NO:42.

35. A substantially purified Elongin C fragment having Elongin A activation activity and capable of binding to Elongin A and/or Elongin B.

36. The substantially purified Elongin C fragment of Claim 35 wherein said Elongin C fragment comprises an amino acid sequence as depicted in SEQ ID NO:46.

37. The substantially purified Elongin C fragment of Claim 35 wherein said Elongin C fragment comprises an amino acid sequence as depicted in SEQ ID NO:47.

38. The substantially purified Elongin C fragment of claim 35 wherein said Elongin C fragment comprises an amino acid sequence comprising the amino acid sequences as depicted in SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:13.

39. A nucleic acid comprising a nucleotide sequence encoding an Elongin C fragment having Elongin A activation activity and capable of binding to Elongin A and/or Elongin B.

40. The nucleic acid of Claim 39, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:46.

41. The nucleic acid of Claim 39, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:47.

42. The nucleic acid of Claim 39, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:13.

43. A substantially purified Elongin C having Elongin activation activity and capable of binding to Elongin A and/or Elongin B.

44. The substantially purified Elongin of Claim 43, comprising an amino acid sequence as depicted in SEQ ID NO:46.

45. The substantially purified Elongin of Claim 43, comprising an amino acid sequence as depicted in SEQ ID NO:47.

46. The substantially purified Elongin C of claim 43 comprising an amino acid sequence comprising the amino acids sequences as depicted in SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:13.

47. A nucleic acid comprising a nucleotide sequence encoding an Elongin C having Elongin A activation activity and capable of binding to Elongin A and/or Elongin B.

48. The nucleic acid of Claim 47, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:46.

49. The nucleic acid of Claim 47, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:47.

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50. The nucleic acid of Claim 47, wherein the nucleotide sequence encodes an amino acid sequence as depicted in SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:13.

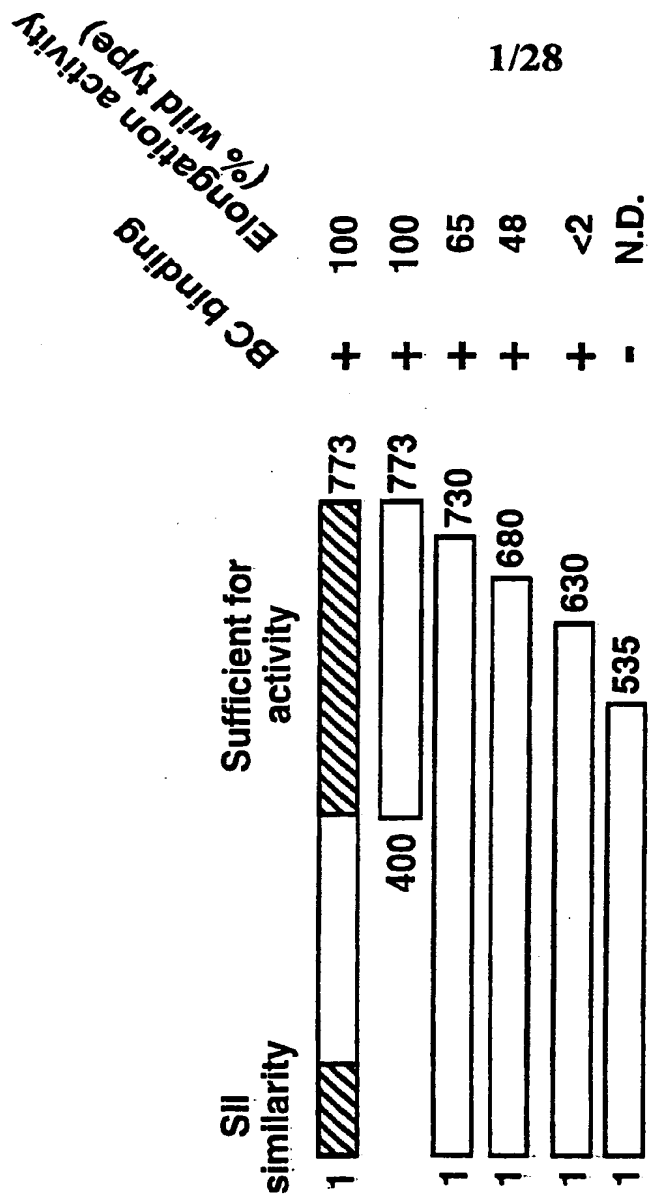


Fig. 1A

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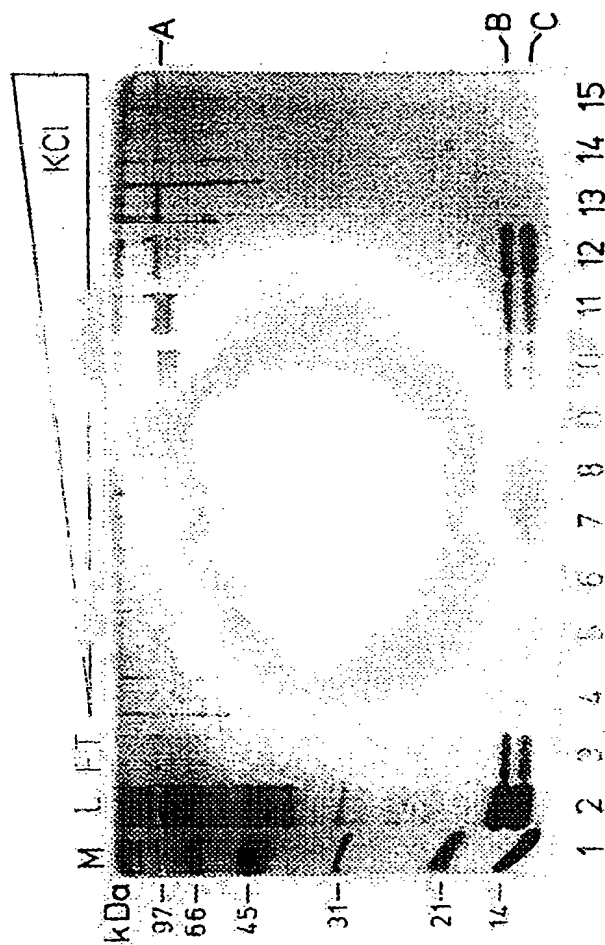


Fig. 1B

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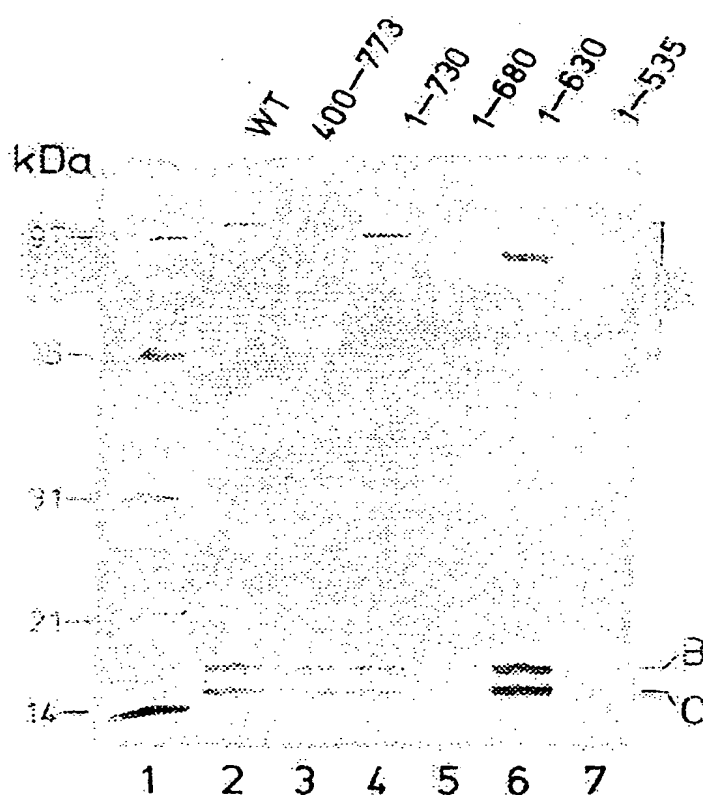


Fig. 1C

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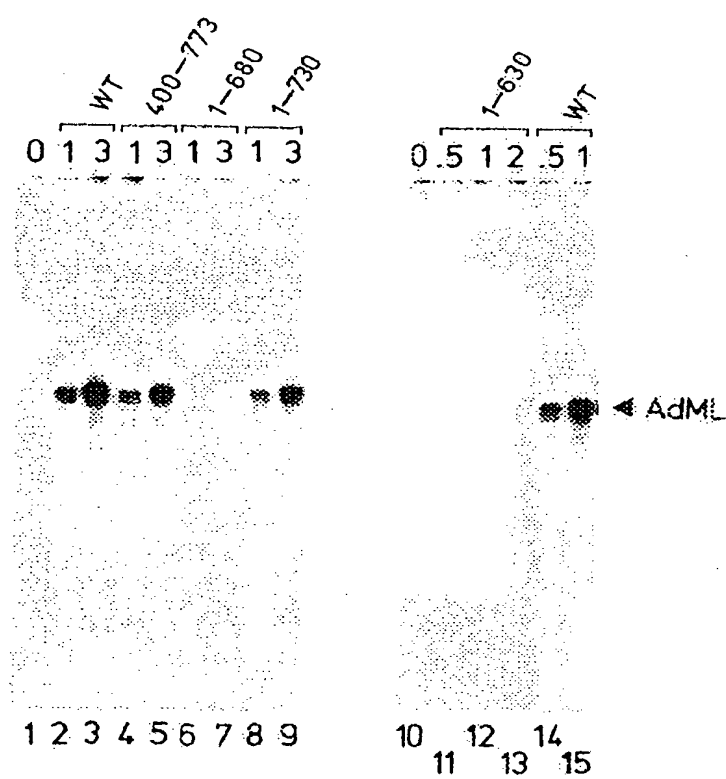


Fig. 1D



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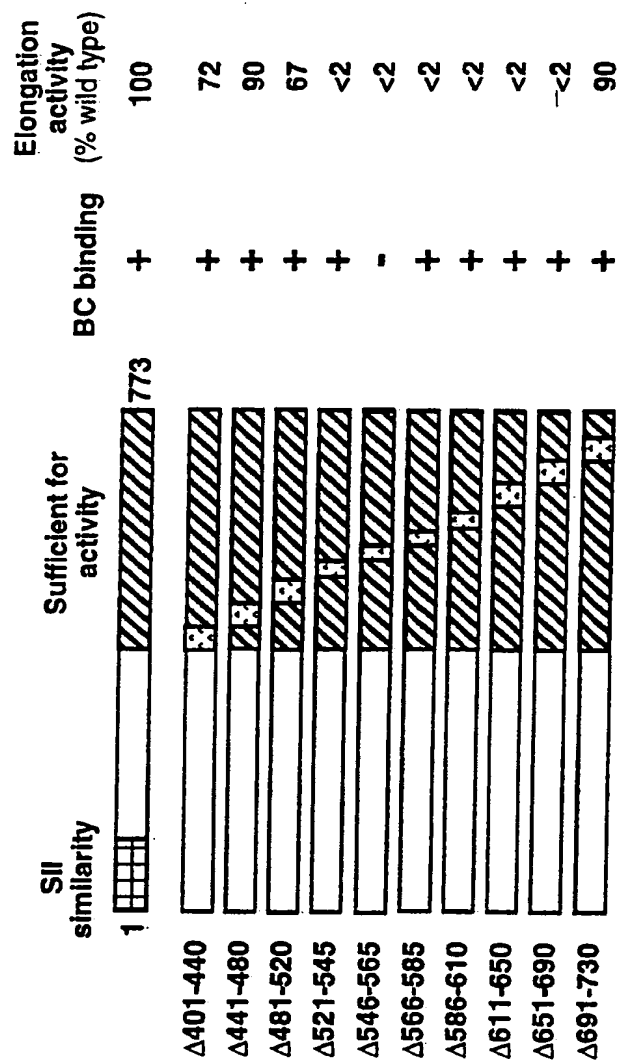


Fig. 2A

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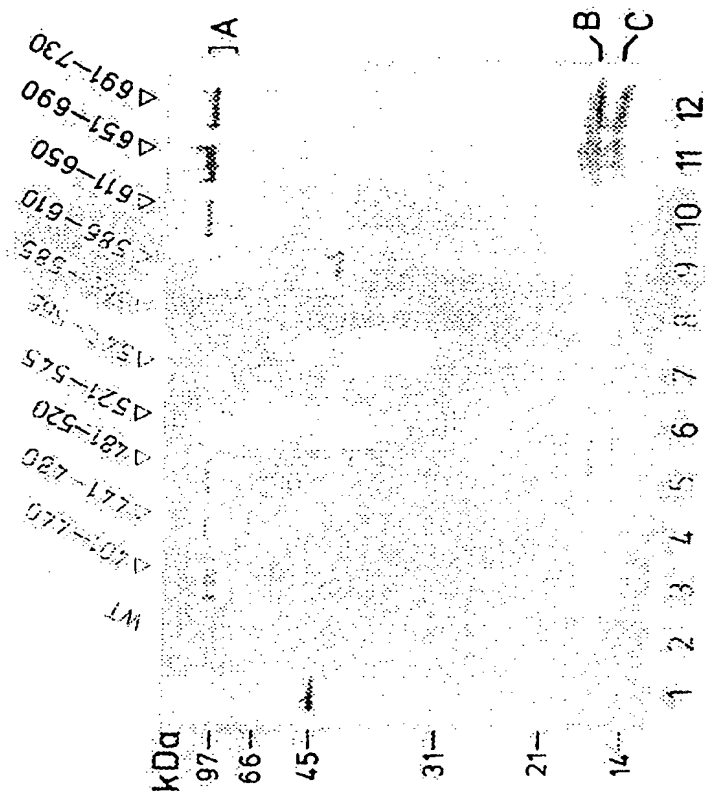
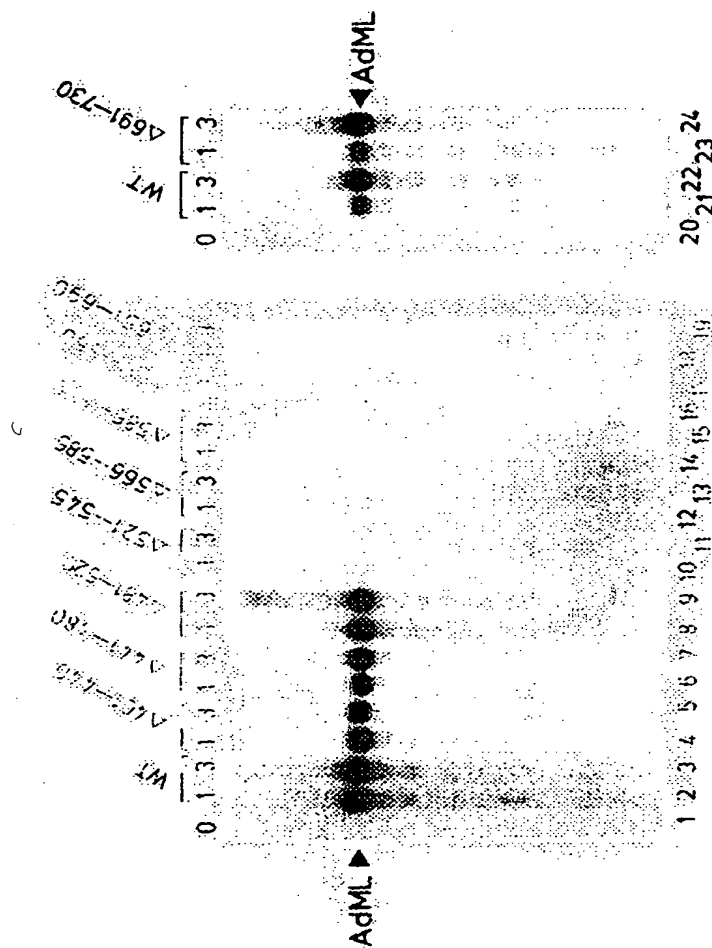


Fig. 2B

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**Fig. 2C**

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**Fig. 3A**



**Fig. 3B**

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Elongation Activity  
BC binding

545 550 555 560 565  
EloA 540 KCAYLPKMTLHQQCIRVLKNNIDSIFEVGG 570  
VHL 148 FANITLPVYTLKERCLQVRSVLVKPENYRRL 178

	+	+	+	+	+	+
wild type	+	+	+	+	+	+
Δ545-548	+	+	+	+	+	+
Δ549-552	+	+	+	+	+	+
Δ553-556	+	+	+	+	+	+
Δ557-560	+	+	+	+	+	+
Δ561-564	+	+	+	+	+	+
Δ565-568	+	+	+	+	+	+

Fig. 4A

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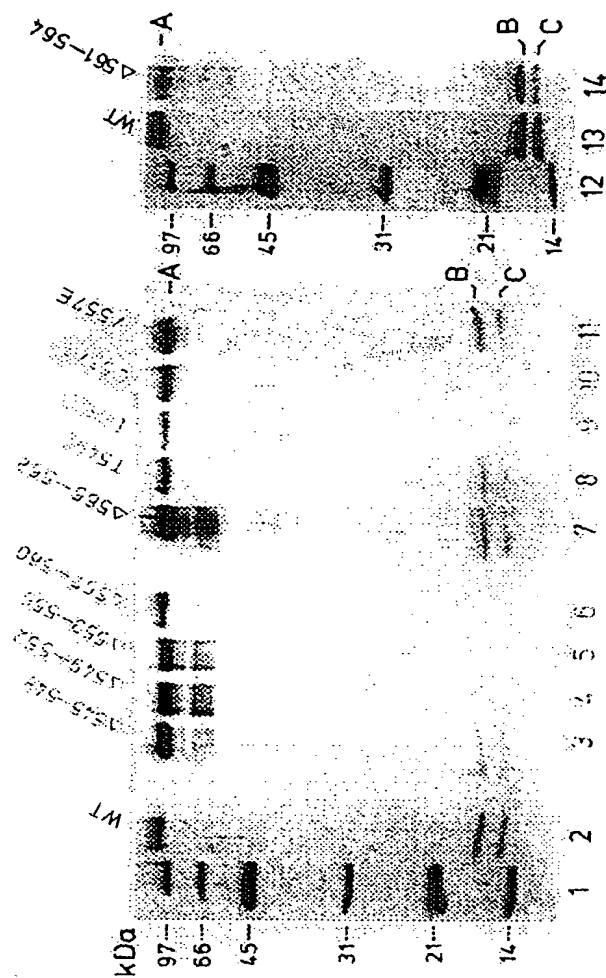


Fig. 4B

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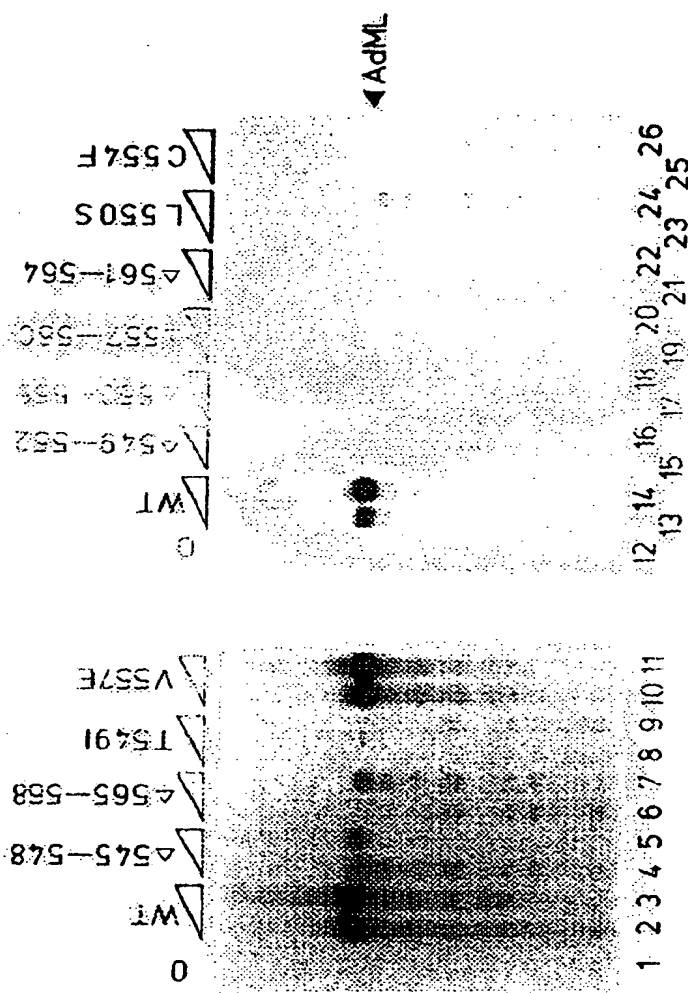
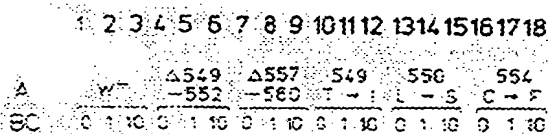
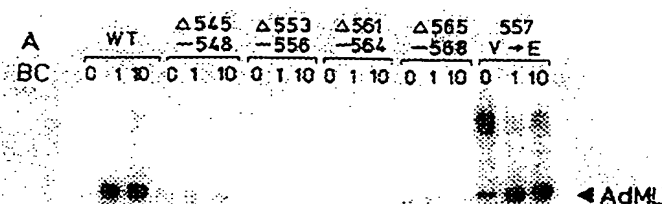


Fig. 5A

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19 21 23 25 27 29 31 33 35  
20 22 24 26 28 30 32 34 36

Fig. 5B



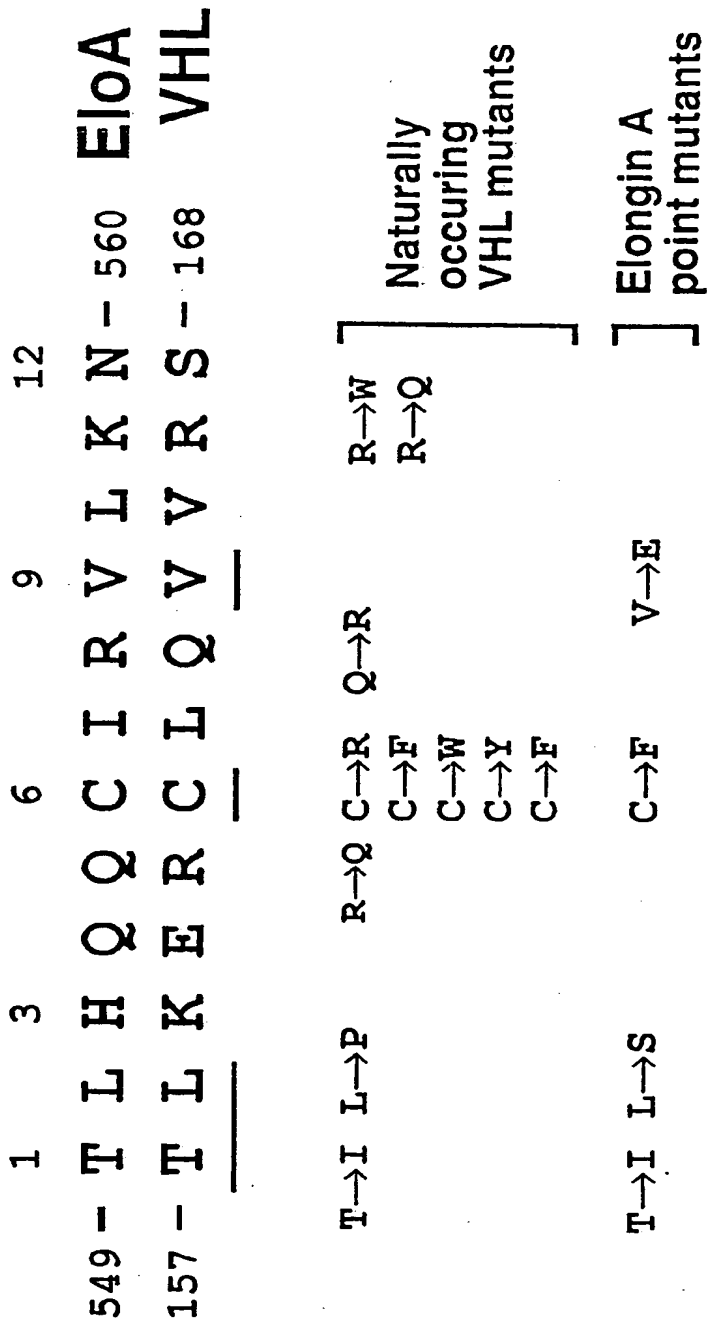


Fig. 6

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Rat C.elegans	MAAATSSALQVV M-PIETDEEKV	EKQAR RRTYEC	AAAN LMNG	PDPK IDPKRA	LKYV LKR	KK[SVLP] YD[LVSP]	ITV --	DILVETGVGK EVFKSADTVQ	TVNSFRKHEQ CVKRYESSPE	60 56	
Rat C.elegans	VGNFAR LAKYAKRVRD	D[VAQW] K[LGGR]	KLV KR--	PVETRNNEAE --EKGGGDD	ADJEHTALKK	QDFFIEKSSNRK ADJEHTALKK	--RPRDW AKKEEVLNDE	FEFATG FEFATG	NYQE AMKSGV	114 112	
Rat C.elegans	SMQA AQSAPRA	SGSQPY TVDYSK	KHR KVV	KLPEILERPHK KRVIEVKKVEPK	VAHCHERRDE PEPVDVHEQQ	VAHCHERRDE PEPVDVHEQQ	ASSS--SMS	WSSSDP YQREHQA	SSDY KD--	174 167	
Rat C.elegans	GHVQSPPPSS	PHQMYTDLR	SPEMDQEPV	SHPKPGKVHS	NTFQDR	LVGS	HLGEHQA	GKGA	234		
Rat C.elegans	VSQNKPKHSS	HKEKRPVDAR	GDEKSSVMGR	EKSHKASSKE	ESRRL	LSSEDS	AKEKL	PSVV	294		
Rat C.elegans	KKEKDREGNS	LKKKLSPALD	VASDNHFKKP	KHKDSEKIKS	DNKQ	SVDSV	DSGRGT	GDPL	354		
Rat C.elegans	PRAKDKVPNN	LKAGEGKVRT	NSDRKSPGSL	PKVEEMDMDD	EFEQ	TMSFE	SYLSYD	QPRK	414		
Rat C.elegans	KKKKVVKTSG	TALGEKGLKK	KDSKSTSKNL	NSAQKL	PKAN	ENKSDK	LQPA	GAEPT	PRKV	474	
Rat C.elegans	PTDVLALPD	IPLPAIQTNV	R	LPSLELIS	SFQPKR	KAFIS	SPQEE	FEFAGF	TGRMNS	KMQ	534 206
Rat C.elegans	VYSGSKCAYL VAGRRKRVG	PKMMTTHQQC EGVSLVSLC	IRVLLKNNITDS QTVLMSHIDM	FEFVGGVTFYS DHFVGIYPIFD	V[EPV] L[EPV]	TERCT bHAS	PDQTYR TDQLRH	EEC LDV	595 266		
Rat C.elegans	NHVLITETDQ NPMLVIEDADJE	LWKVHCHRDIF MFHEMVSRIEF	K--EERPEEY PKYANR	ESWREMYLR WIREMYDRL	--QDAREQ VEKKQK	KEND	R[RL] K[LEM]	TNNITR TSRIG	648 326		
Rat C.elegans	SAHANKPKGR KNSAQSQGR	QAKMAFVNSV QTMVJ	AKPRD	VRRR	QEKFGT	GGAA	VPEKVR	IKIPA	PYITGS	SHVP	708 363
Rat C.elegans	SNSSSFS MSATPISALQL	ST--PEELAYIE SQARKNVKIE	QPS--TSSA QKALRITIP	HLAPWA RGGGVPS	SSSV TSR	SYDPR	KPP--	--AVKK	AP	757 423	

Fig. 7

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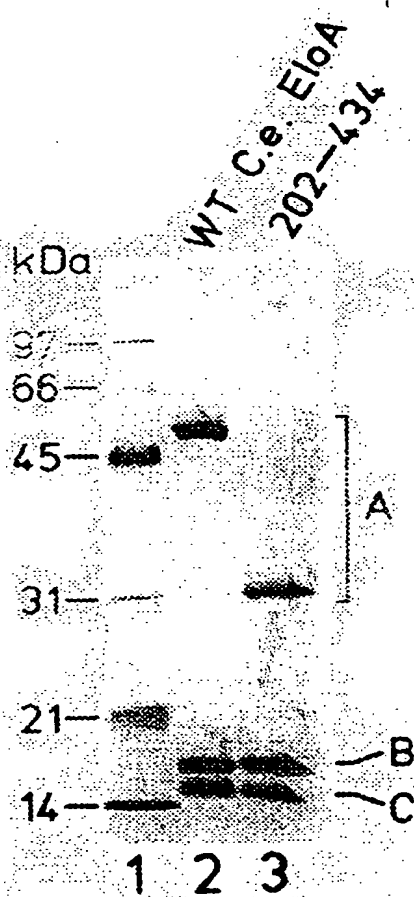


Fig. 8A

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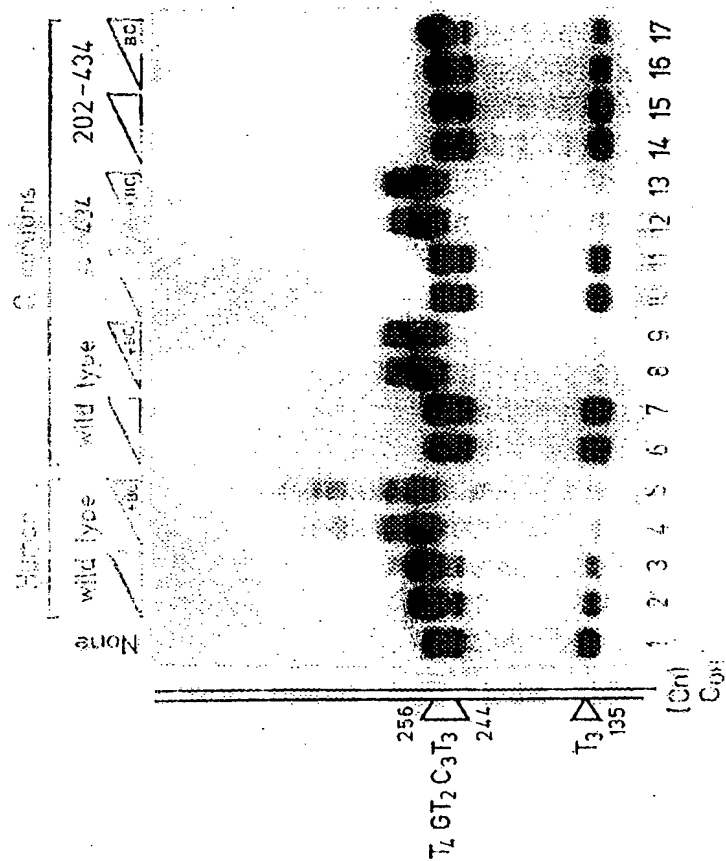


Fig. 8B

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1 2 14 18 22 28 42 56 70 84 98 112  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(15-112) :  
 M-HHHHHHND-DAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(19-112) :  
 M-HHHHHHND-VKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(23-112) :  
 M-HHHHHHND-SSQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(29-112) :  
 M-HHHHHHND-PIVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(57-112) :  
 M-HHHHHHND-TN8VNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1-97) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1-83) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(431-30) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(431-40) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(441-50) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(451-60) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(461-70) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(471-80) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(481-90) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(491-100) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A19-21) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A1-26) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A1-27) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A128-30) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A189-91) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A192-94) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A195-97) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A198- ) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A1101-103) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A1104- ) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A1-109) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC  
 C(1A110-112) :  
 M-HHHHHHND-DOBEKTYGCEGPDAMTVKLISDQCHFTVKEHAL7SOTIKAMLSQPCQPAENETHEVNPRI8P8VLSKVCHVPTTKVYTHNSSTEIP8PIAP8IALELLMAANFLDC

Fig. 9

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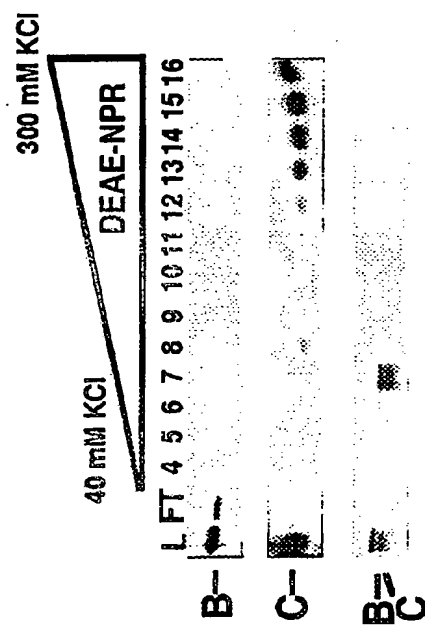


Fig. 10A

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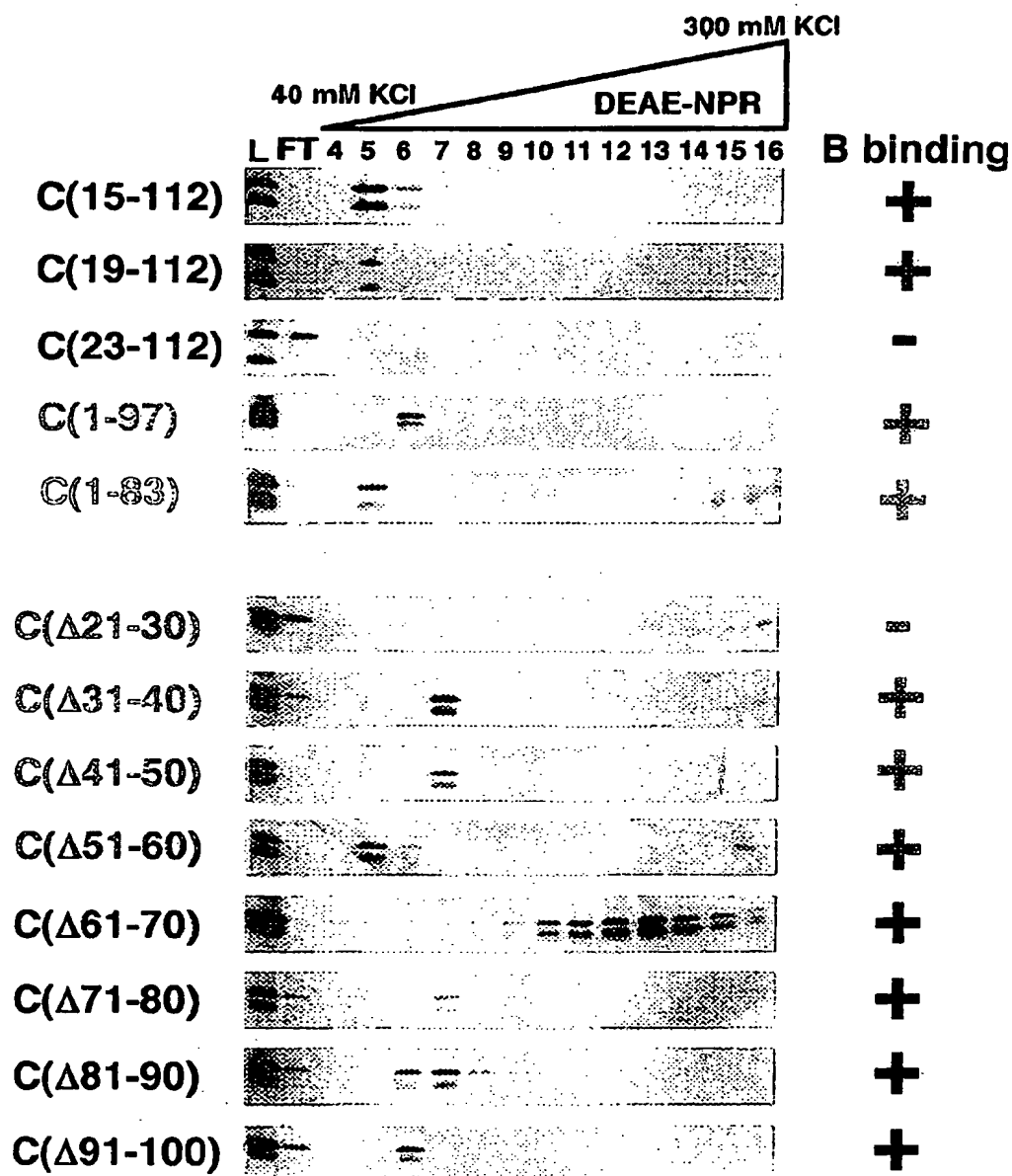


Fig. 10B

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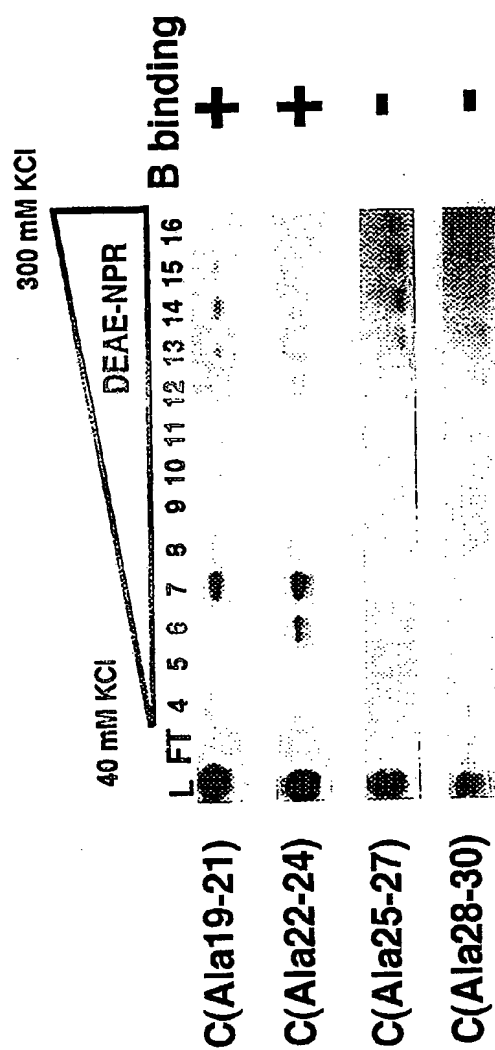


Fig. 10C



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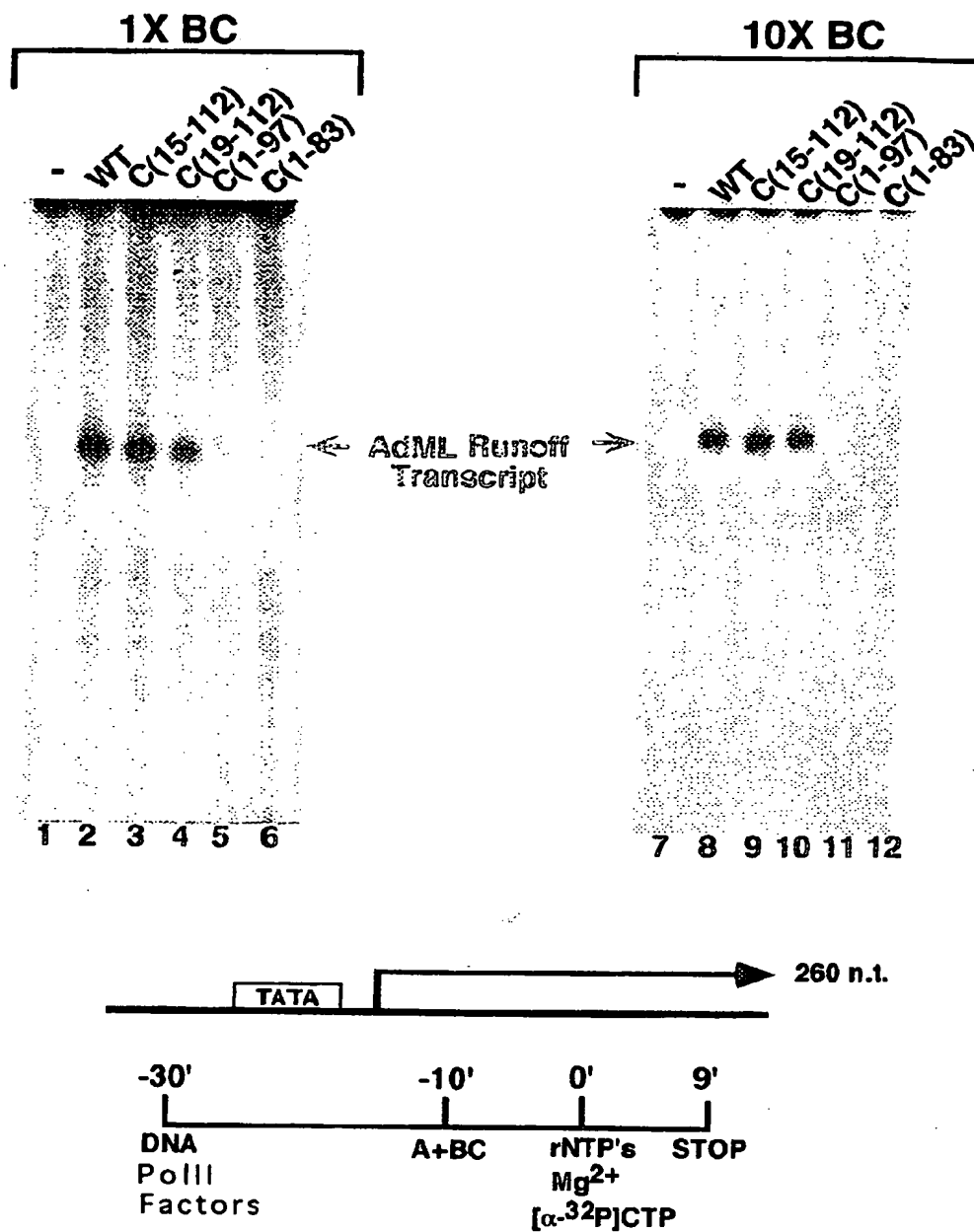


Fig. 11A

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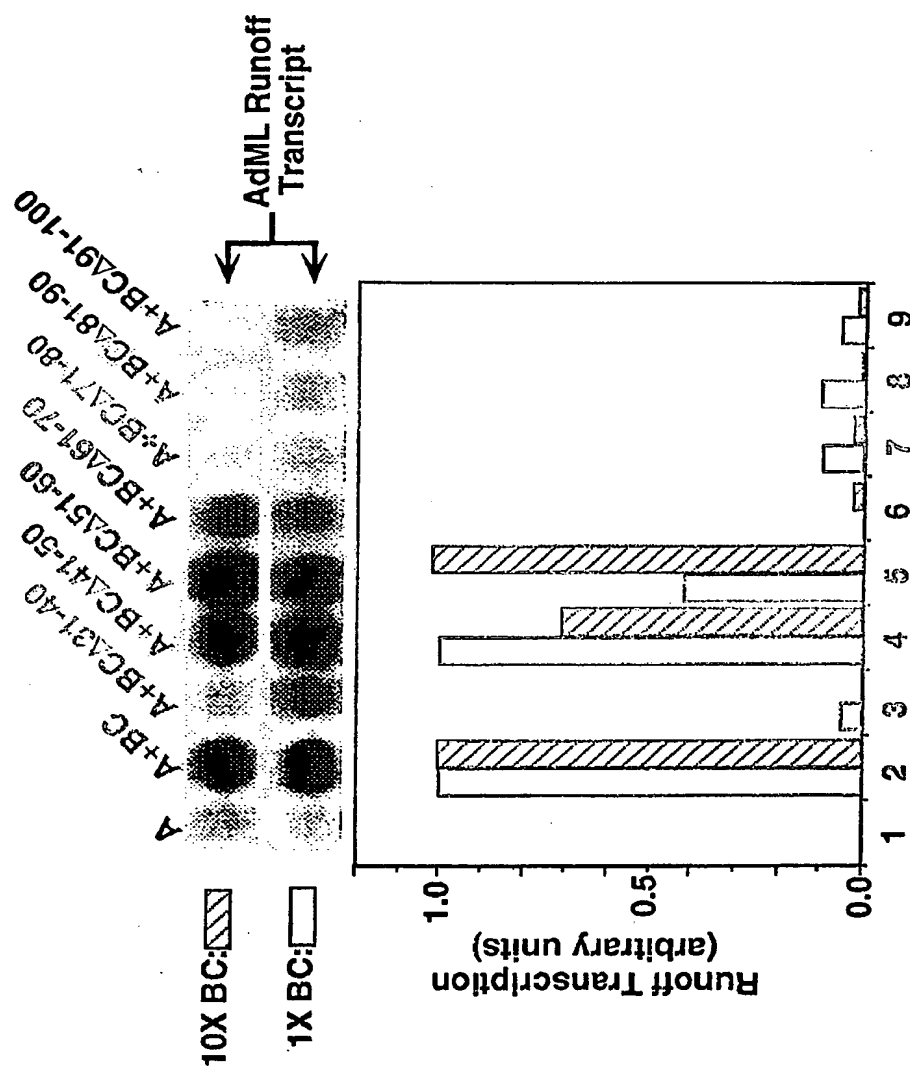


Fig. 11B

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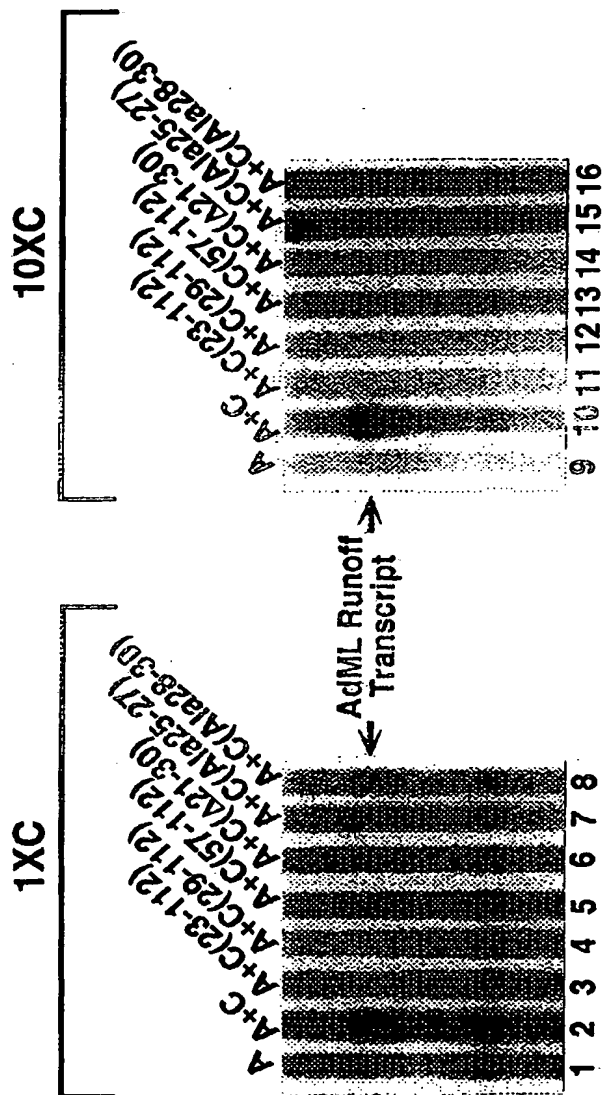


Fig. 12A

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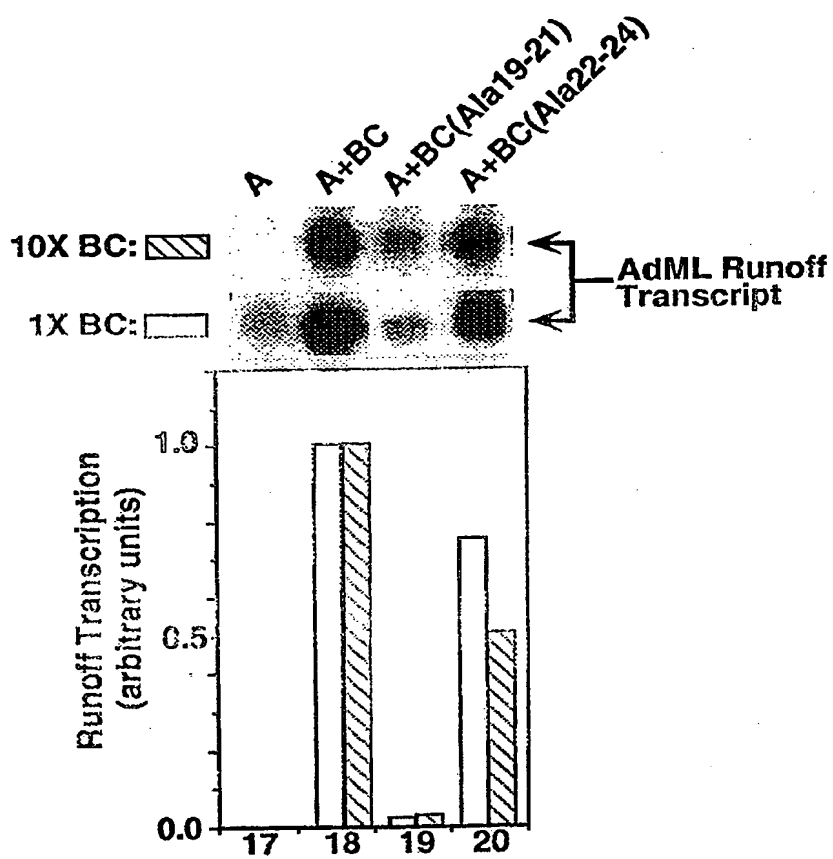


Fig. 12B

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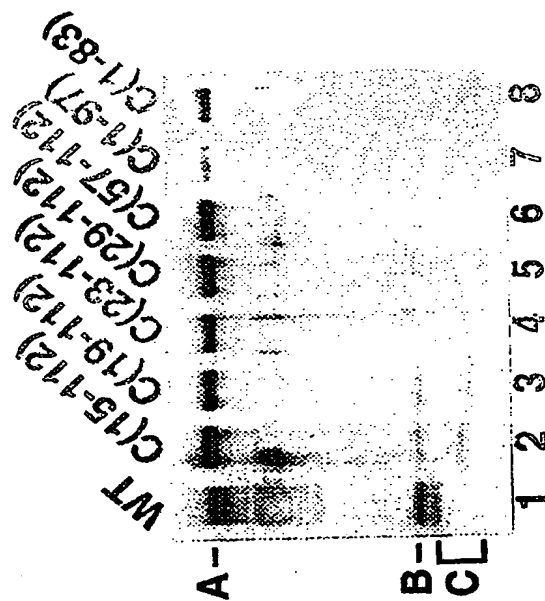


Fig. 13

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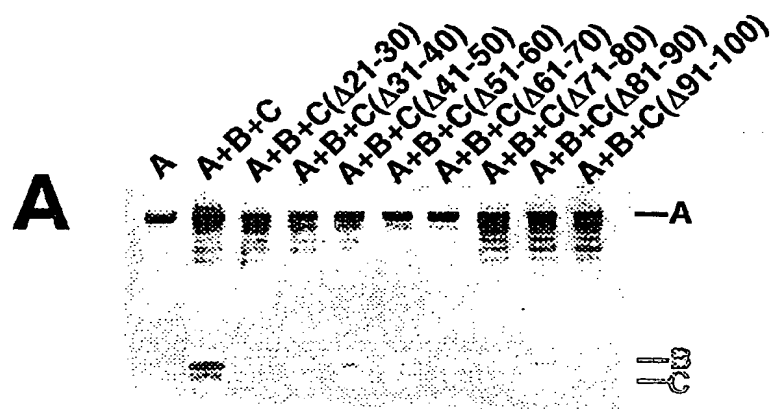


Fig. 14A

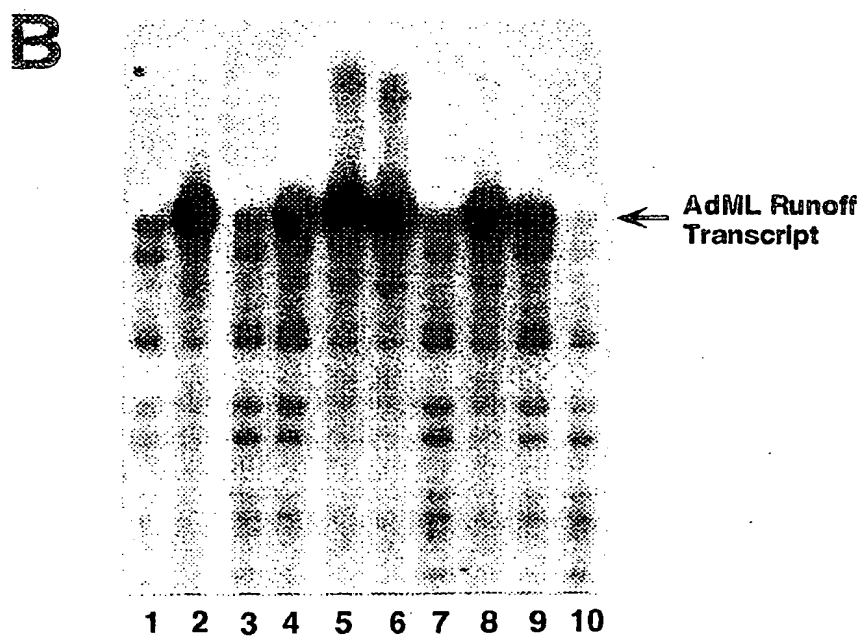


Fig. 14B

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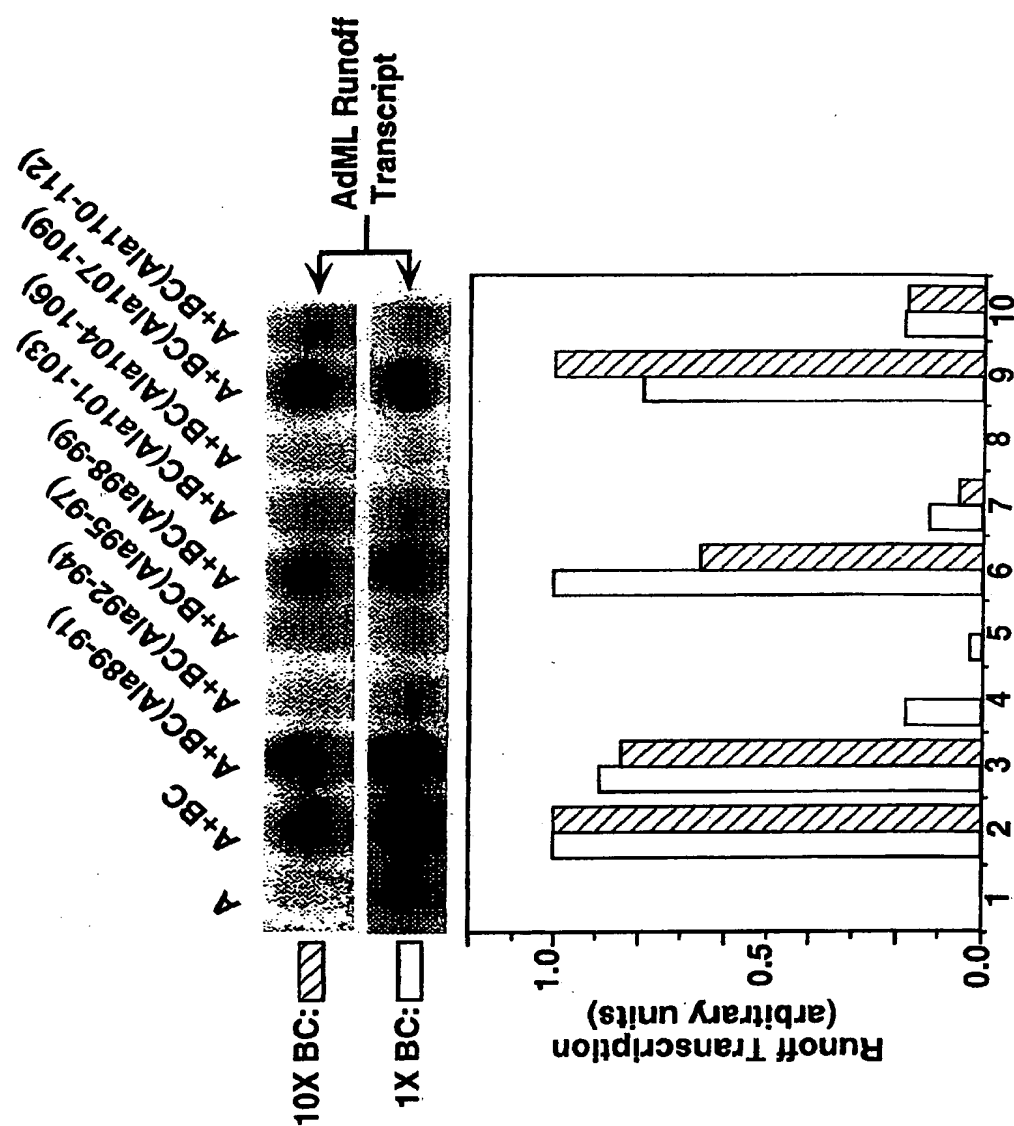


Fig. 15

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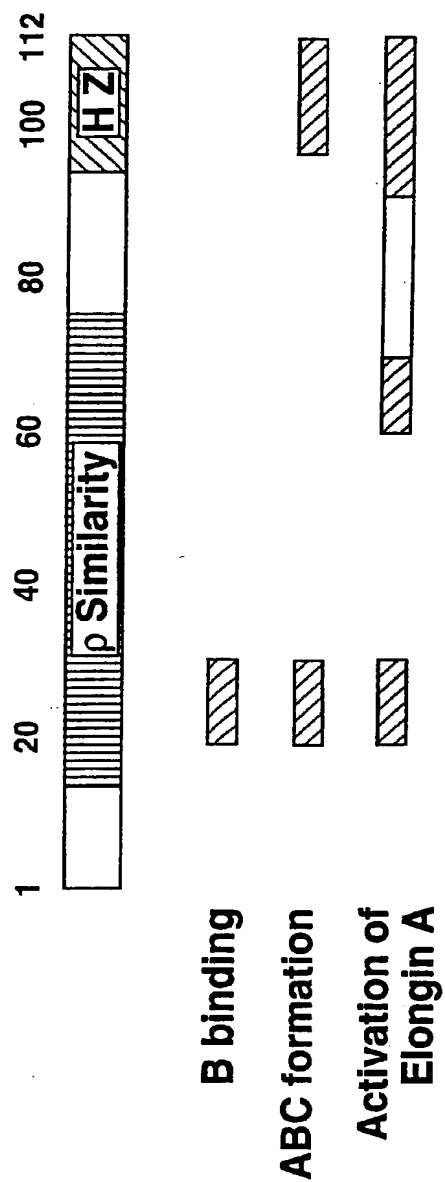


Fig. 16



# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 97/17992

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 6 C12N15/12 C07K14/47 C07K14/435		
According to International Patent Classification(IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 6 C07K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the International search (name of data base and, where practical, search terms used)		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 655 498 A (OKLAHOMA MED RES FOUND) 31 May 1995 see abstract see page 25 - page 27 see page 28 - page 29	17-34, 43-50
Y	---	1-16, 35-42
X	ASO T. ET AL.: "Elongin (SIII): a multisubunit regulator of elongation by RNA polymerase II." SCIENCE, vol. 269, 8 September 1995, pages 1439-1443, XP002023196 see abstract see page 1443; figure 6 --- -/---	1,2
<div style="display: flex; justify-content: space-between;"> <span><input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.</span> <span><input checked="" type="checkbox"/> Patent family members are listed in annex.</span> </div>		
<b>* Special categories of cited documents:</b>		
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&amp;" document member of the same patent family</p> </div> </div>		
Date of the actual completion of the international search  <div style="text-align: center; font-weight: bold;">11 February 1998</div>		Date of mailing of the international search report  <div style="text-align: center; font-weight: bold;">25/02/1998</div>
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  <div style="text-align: center; font-weight: bold;">Lejeune, R</div>

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 97/17992

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE SWISSPROT YRL4_CAEEL (AC 009413), 1 October 1996 SWINBURNE J.: "HYPOTHETICAL 49.2 KD PROTEIN R03D7.4 IN CHROMOSOME II" XP002055270 see sequence</p>	33, 34
Y	<p>TAN S. ET AL.: "Dissection of transcription factor TFIIF functional domains required for initiation and elongation." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 92, 20 June 1995, pages 6042-6046, XP002055269 see abstract see page 6043; figure 1</p>	1-16, 35-42
P, X	<p>WO 97 09426 A (OKLAHOMA MED RES FOUND) 13 March 1997 see page 63 - page 64 see page 70 - page 72 see page 42, line 25 - line 30</p>	1-34, 43-50
P, X	<p>ASO T. ET AL.: "The inducible elongin A elongation activation domain: structure, function and interaction with the elongin BC complex." THE EMBO JOURNAL, vol. 15, no. 20, 15 October 1996, pages 5557-5566, XP002055267 see the whole document</p>	1-34
P, X	<p>TAKAGI Y. ET AL.: "Characterization of elongin C functional domains required for interaction with elongin B and activation of elongin A." THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 41, 11 October 1996, pages 25562-25568, XP002055268 see the whole document</p>	35-50